The New England
Journal of Medicine

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Volume 230 June 8, 1944 Number 23

MEDICAL SERVICE IN INDUSTRY*

DWIGHT O'HARA, M.D.†

BOSTON

THE title assigned to me suggests that there is a field in industry that medicine and surgery may enter and expand. Although this is undoubtedly true, the title might more appropriately read "Industry in Medical Service," thus indicating what is an even greater opportunity — that is, for industry to enter into and expand the field of medical service to its employees. I believe this because in the recent past and at the present time there are apparently more physicians ready and willing to enter industrial employment than there are industrial employers ready to engage them. The Committee on Industrial Health of the Massachusetts Medical Society has definitely found this to be so, even in this period of unprecedented industrial activity, for during the last year and a half it has received from physicians a dozen requests for industrial jobs for every one it has received from industrialists looking for physicians.

In this apparent discrepancy between supply and demand there are several noteworthy factors. In the first place, the supply pool, although it contains the names of several outstanding physicians and surgeons in the Commonwealth, is not a good random sample of the medical profession of the State. This is because the vigorous, well-trained physicians of today are apt to be too preoccupied in military and other services to be looking for work. In the second place, the industrialists are not generally aware of the potential usefulness of modern medical service in their business relations with their employees. They do not appreciate that the physiologic principles on which the upkeep of the human machine depends are as important as the mechanical principles on which they keep up their lathes and looms. In the third place, neither the physicians nor the industrialists generally know exactly what they are looking for, because industrial medicine is anything but cut and dried. The field is not so highly specialized as it has sometimes been represented to be; it needs further clarification as a specialty, if indeed it does not need to be reappraised as another form of the general practice of medicine.

There are now many types of industrial practice, and there are also many types of physicians engaged in it. They all have in common, however, certain interests that do not permit their straying as far from the fundamental principles and disciplines of medicine as many of the more highly organized specialists may. Within the last few years I have repeatedly heard candidates in Part III of the National Board Examinations request leniency or defiantly refuse to answer questions on the ground that they were not interested. This apathy was due to their intention to devote their talents to psychiatry, radiology or some other special field. They blandly assume that such interests release them from further responsibility in their wider profession. This attitude is sometimes found among third-year and fourth-year medical students, although they are usually discreet enough to keep it to themselves at that stage of their careers. The fact that such limitation of responsibility actually permits a specialist to command a larger income is one of the inconsistencies with which modern medicine has vested itself, and on account of which the cost of medical care has arisen in the large centers of population. The extent to which it has taken over the public's thinking about medicine is well known to those who have questioned the motives of the young men who now seek admission to our medical schools. In the most recent block of such young men whom I have questioned, for example, two out of twenty-one had already decided that they were going to become brain surgeons.

Of course everyone appreciates the technical advances that have paralleled this narrowing process. The primary point to be made in connection with it is that no such atrophy of medical and surgical interest or activity is compatible with the practice of industrial medicine. Certain industries have their

*Presented at the War Session of the American College of Surgeons, Springfield, Massachusetts, March 20, 1944.

†Professor of preventive medicine, Tufts College Medical School; visiting physician, Boston City Hospital; physician-in-chief, Waltham Hospital.

own peculiar and often specialized problems, but the industrial physician must be ready to be all things to all men most of the time. He must be able to do the thing that general practitioners have always done so well: to decide quickly what is important and urgent, and to use pleasing and soothing devices for the rest. Although these soothing devices have frequently been amusing, they have admirably served their purpose, which is to get the patient out of the way so that the physician can get on with his work. In large plants with well-organized medical departments the industrial physician has greater resources than has the private practitioner, but it is just as necessary for him — or for someone on his staff — to get the employee back to his job as it is for the private physician to get the patient out of his office. My first thought about medical service in industry therefore is that it should be looked on, not as a new specialty in the conventional sense, but as a new application of the general practice of medicine.

The medical department of a large plant should and usually does provide a unit with which the family physician can co-operate with complete understanding and confidence. Such co-operation between industrial and family physicians is of the utmost importance in meeting the many problems now facing industry. Among these may be mentioned the breaking in of inexperienced workers, the adjustment of handicapped people to suitable jobs, the frequency rate of accidents, absenteeism following accidents or illness and the incidence of preventable illness. The medical department is interested in all these things, but they are closely and inexorably connected with housing standards, home environments, sickness in the family, previous illnesses and incapacities of workers, shopping, amusement and transportation facilities; in short, the things with which the family physician is traditionally familiar and concerning which he is often consulted. It may thus be said that there are at least two sectors of the home front of industrial health. The medical departments of large industries are universally anxious to correlate the medical command on these sectors, and may be counted on to come more than halfway in any movement toward unification of medical outlook. Most family physicians are now convinced that this is so; if they are not, they are lacking in experience. The private physician may now be expected to work for the welfare of his patient with the medical departments of the large plants as conscientiously as he does with the public-health authorities.

In the small plants on the other hand, where the opportunity to support a medical department is usually lacking, there is not apt to be an organized interpretation of medical viewpoints for the management, and the whole subject of medical service gets off to a poor start. Traumatic surgery is generally well cared for and is well followed up by the agents of the insurance companies. Headaches and other minor complaints may be given symptomatic treatment, but there the service rests. The problems referred to in the preceding paragraph are almost unknown because they are not recognized, whereas absenteeism, which cannot escape recognition, becomes just "one of those things." There may be a nurse or two in attendance; attending physicians and surgeons are generally called when needed and are usually paid on a fee basis. Representatives of such industries probably do not attend or do not know about the periodic meetings where industrial health is discussed. Obvious hazards are promptly corrected whenever attention is drawn to them, as it not infrequently is by a serious accident. It is true that the agents of these small plants can frequently point to excellent or even "perfect" safety scores, but such records perhaps depend on the relatively small number of employees involved or on the nonhazardous character of the particular trade that they ply. Of course many small industrial establishments are thoroughly healthful places in which to be employed. The chances are, however, that they are healthful places because someone not only has made an effort to make them so but also is attempting to keep them so.

The importance of these small plants in Massachusetts rests on the fact that their employees aggregate approximately three quarters of the men and women industrially employed within the Commonwealth. The problem is therefore large and complex, and because of the many small and diversified units into which it breaks down, it is a difficult problem. It is difficult from the employer's point of view because he cannot visualize a private medical department within his small plant any more than he can a private fire department. It is difficult from the physician's point of view because he cannot easily concentrate on the preventive aspects of an assignment that is really a very small part, and not at all an urgent one, of his total responsibility. Unless the employer or his physician can become enthusiastic about his admittedly little share of this big problem, not much progress can be made. If such progress is to be accomplished it is necessary to find an *enthusiast* — whether he is a manager, a physician, a foreman, a nurse or a janitor. He may be any intelligent person who will deliberately view a plant and ask himself about the possibilities of injury from fluids, fumes, dusts or metals. If his survey raises any suspicion that the worker's health is being undermined, the hunt is on. The physician who has this enthusiasm and interest is the ideal hunter. If he has practiced medicine successfully he will enjoy in a greater degree than do others, the confidence of those who know him, and as a physician he will have a natural knowledge of physiology on which he may build and through which he may be able to answer many primary questions. Indeed, the general practitioner may have

an approach that gives him fundamental advantages over other persons, even over specially trained industrial hygienists. No person who is not enthusiastic about the idea as a whole, however, will be likely to succeed in producing results.

There is a most useful group of people who are now organized and available in almost every community — the people who variously call themselves district, visiting or community-health nurses. They are in a particularly strategic position to promote industrial health in small plants, especially if the casually employed plant physician will give them the "green light." They are not expensive or intrusive; they are familiar and in daily touch with public-health regulations; they enjoy the confidence of the people and of the medical profession; if given slight encouragement by a few small plants they can afford to assign one of their staff to inform herself specifically in the principles of industrial hygiene. I have been much interested in watching the evolution of such a district nursing group in a city of 40,000 population with which I am familiar. They have successively trained different persons on their staff, so that in addition to what they call a "diabetic nurse" and a nutritionist they now have two members who have been trained in the elements of industrial hygiene. One of these nurses recently learned, almost surreptitiously, of a skin blemish that on tactful investigation was found to be part of a widespread epidemic of cutting-oil dermatitis among a group of women machinists whose thighs were exposed through absorbent overalls. Because their hands and faces were not involved these workers had not complained and had kept the condition of their legs to themselves. Medical advice led to proper protection and remedial measures, which promptly ended the trouble.

The nurse has traditionally held an intermediary position between the physician and his clientele; she can make or ruin him professionally almost as easily as his wife can make or ruin him socially. The nurse can as readily promote or neutralize industrial health; in the large and medium-sized plants she has already demonstrated her great value and has successfully promoted the health of the workers in many ways. In the small plants she must, however, be alert and resourceful; she must have a broad horizon, an active imagination and vigor if she is to keep herself from settling back into a soft corner, where she has to knit and read while she waits for the opportunity to paint iodine on a hangnail. It seems that the small plant must be guarded against this leisurely sort of nursing routine, and for this reason the district nursing type of setup is extremely appealing. These district nurses have the added advantage that they are in close touch with the homes, the schools and the families of the men and women with whom they work. It is again the same advantage that the general practitioner enjoys — that of not being limited by the fence that surrounds the plant. The scope of industrial medicine, like that of preventive medicine, can have no such limit.

It is doubtful whether the managements of three or four different small plants could agree for long on the terms under which they might jointly employ an industrial nurse, but there is no doubt at all that they could all deal satisfactorily with an independent district-nursing organization. The independent organization, by working on an hourly basis, can adjust the service to the times that will meet the needs of each plant, thus relieving the plant managers of the vexing problem of deciding whether they should employ their nurses on full-time, half-time or quarter-time periods. It should appeal to the economic sense of businessmen to be able to buy only what they need. This is the best solution I have yet seen in operation for giving to small and moderate-sized industrial enterprises something that they can afford and that their employees are entitled to.

Summary

Although single industries may expose their workers to special hazards, the practice of industrial medicine is a form of the general practice of medicine.

At the present time medical service is well organized in many of the large plants. Private practitioners should co-operate with the medical authorities of these plants as they do with public-health authorities.

Medical service in the small plants in Massachusetts is not well developed. It has been and can be developed by district-nursing groups in an efficient and economic manner. Private practitioners may well take the lead in this matter.

5 Bay State Road

THE CLINICAL SIGNIFICANCE OF BACTERIURIA IN PATIENTS WITH SPINAL-CORD INJURIES*

DANIEL BADAL, M.D.,† DONALD MUNRO, M.D.,‡ AND MARION E. LAMB§

BOSTON

ALTHOUGH it has long been recognized that infection of the genitourinary tract is one of the most prolific causes of death and disability in patients with spinal-cord injuries, we have been unable to find any data on the incidence of the different types of infecting agents, and in particular could discover nothing in regard to the clinical significance of a bacteriuria and the relation its presence has in such cases to the production of symptoms of cystitis, ureteritis or pyelitis. In the course of establishing the effectiveness of tidal drainage as a means of controlling infection of the genitourinary tract, it shortly became apparent that an effort must be made to differentiate a bacteriuria and an active infection of the tract. As integral parts of this problem the effectiveness of various urinary antiseptics had to be determined, the influence of an indwelling catheter on the prolongation of bacteriuria ascertained, the incidence of bacteriuria in normal uncatheterized persons settled, and finally a method developed by which the urine could be conveniently and accurately cultured and at the same time overgrowth of any one contaminant sufficient to mask the presence of others prevented. This paper presents our experience with these various problems.

METHOD OF CULTURE

It was obvious that before any such investigation could be undertaken a proper method of culture must be developed. Moreover, to be significant the urine to be cultured had to be bladder urine uncontaminated by passage through the urethra. It was evident that to meet this requirement catheterization would be necessary. Moreover, some method must be adopted to minimize the effect of the contamination of the bladder urine by the transference of urethral bacteria on the catheter as it was inserted. The method that was finally evolved and that has proved satisfactory for the last eight years follows. It is reliable, dependable and accurate. The cultured plates are easy to read and are not overgrown by the more prolific bacteria.

After washing the external meatus with soap and water a new sterilized catheter is inserted in the bladder. The use of a new catheter decreases the chances of contamination slightly and is preferable but not essential. Catheters that have been in use so long a time as to have become encrusted with urinary salts should not be employed. The bladder is emptied and irrigated gently with a sterile 0.5 per cent solution of acetic acid, which is then removed. The catheter is fastened in place and clamped off, and the bladder is allowed to fill from the kidneys for two hours. At the end of this time the catheter is opened and 10 cc. of urine is allowed to wash through the catheter, which is then closed off again. The outer wall of the catheter is sterilized by painting the area between the meatus and the clamp with full-strength tincture of iodine. This is allowed to dry, a sterile hypodermic needle attached to a sterile syringe is plunged through this area into the lumen of the catheter, and urine is withdrawn therefrom into the syringe. One drop of this urine is placed on a blood agar plate and spread over half the plate with a sterile loop. The loop is then resterilized and the other half of the plate is subcultured from the urine that has been spread over the first half. The ideal way is to plate the urine at the patient's bed with due care to prevent contamination, but if this cannot be done the syringe and needle should be carried at once to the bacteriological laboratory and the plating carried out there. Any delay in making the culture alters the relative amounts of the various bacteria in the urine and leads to confusing overgrowths on the plate. An eosin-methylene blue plate and blood broth may be used. We have not made anaerobic cultures.

Urine cultures have been made by this method on 53 out of 169 cases with all levels of spinal-cord and cauda-equina injuries. Five hundred and seventy-eight cultures have been examined (Table 1). Table 2 shows the number of cultures per patient, and Table 3 gives certain data relative to the first culture made and to cultures made within twenty-four and forty-eight hours after the injury, as well as the total number of various bacteria

TABLE 1. *Total Number of Urinary Cultures.*

TYPE OF SPINAL INJURY	NO. OF CASES CULTURED	NO. OF CASES NOT CULTURED	TOTAL CASES	TOTAL CULTURES
Cervical:				
Living	24	31	55	311
Dead	4	42	46	24
Thoracolumbar:				
Living	8	10	18	118
Dead	6	17	23	62
Cauda-equinal:				
Living	11	14	25	63
Dead	0	2	2	0
Totals	53	116	169	578

*From the Mallory Institute of Pathology and the Department of Neurosurgery of the Boston City Hospital.

†Formerly, assistant to the resident, Neurosurgical Service, Boston City Hospital.

‡Assistant professor in neurosurgery, Harvard Medical School; associate surgeon, Boston University School of Medicine.

§Bacteriologist, Boston City Hospital.

grouped according to the class of case. The first culture made in each patient showed a single type of organism in only 20 cases. There was no growth in 27. Table 4 shows the total number of cases in which the different kinds of bacteria were cultured. It is apparent that *Proteus vulgaris*, *Escherichia coli*, alpha-hemolytic streptococci, enterococci and staphylococci are the significant bacteria. It should also be noted that although proteus and colon bacilli predominated in the cultures, alpha-hemolytic streptococci and enterococci were present at one time or another in the bladder of as many patients as showed the former two bacteria. It also appears probable in the light of this there were too many uncontrollable factors to make them suitable subjects. In addition to plating 1 drop of urine, cultures in blood broth were made of 1 cc. and 5 cc. of urine in order not to miss the more dilute concentrations of bacteria. Growth on the plates was reported as follows: four to ten colonies, +; the most profuse growth ++++, with ++ and +++ in intermediate types of growth. All the cases that showed positive cultures in 1 drop of urine also showed positive cultures in 1-cc. and 5-cc. amounts. Diphtheroids were grown six times in 5 cc. of urine only. They appeared alone five times and in combination with *Staphylococcus albus* once. When they appeared alone there was no other growth in any dilution. *Staph. albus* was grown alone once and in combination with an alpha-hemolytic streptococcus once; and an alpha-hemolytic streptococcus was grown alone twice, but in 1 cc. and 5 cc. of urine only. When present at all, *Staph. albus* showed only 1 colony per plate three out of four times and a + growth once. *Esch. coli* was present in ++ amount once, as were alpha-hemolytic streptococci in + amount; *Staph. citreus* showed only one colony per plate once.

TABLE 2. *Number of Urinary Cultures Per Patient.*

Type of Spinal Injury	1	2	3	4	5	6–10	11–20	21–30	31–40	41–50	Over 50	Total Cultures
Cervical:												
Living	1	5	1	2	1	5	5	0	1	2	1	24
Dead	2	0	0	0	0	1	1	0	0	0	0	4
Thoracolumbar:												
Living	2	0	0	1	1	1	1	1	0	0	1	8
Dead	1	1	0	1	0	1	1	0	1	0	0	6
Cauda-equinal:												
Living	2	1	1	2	1	2	2	0	0	0	0	11
Dead	0	0	0	0	0	0	0	0	0	0	0	0
Totals	8	7	2	6	3	10	10	1	2	2	2	53

TABLE 3. *Results of Urinary Cultures.*

Organism	Growth			Type of Spinal Injury						Total Cultures
				Cervical		Thoraco-lumbar		Cauda-equinal		
	First culture	24 hr. after injury	48 hr. after injury	Living	Dead	Living	Dead	Living	Dead	
P. vulgaris	4	0	0	106	4	62	44	33	0	249
Esch. coli	4	0	0	160	11	44	32	35	0	282
Enterococci	1	0	0	37	8	30	7	9	0	91
Alpha-hemolytic streptococci	2	1	0	78	8	20	17	26	0	149
Staphylococci	2	0	0	67	13	37	7	20	0	144
Other streptococci	0	0	0	6	1	3	0	3	0	13
Ps. pyocyanus	0	0	0	13	1	4	4	3	0	25
Diphtheroids	0	0	0	11	0	3	4	2	0	20
Miscellaneous	7	0	0	40	2	16	9	9	0	76
No growth	27	3	2	27	1	0	1	1	0	30

fact and the figures cited above that in this type of case *Pseudomonas pyocyaneus*, nonhemolyzing streptococci, a miscellaneous group of bacteria and possibly diphtheroids may well be contaminants of the various cultures rather than true inhabitants of the urethra or the bladder urine.

Controls

In an endeavor to determine the incidence of bacteriuria among normal persons, 50 men were selected for urinary culture (Table 5). Before selection a careful history was taken and a thorough physical examination was made. Only those patients who had a history of never having had any genitourinary disease or injury and whose condition at the time of examination had no relation to the genitourinary tract were included. No women were examined because it was believed that

Clinical evidence of bacteriuria, with or without evidence of infection in the form of a rise in temperature and leukocytes in the urine, was investigated in this control group. No patient had an abnormal temperature. In looking for leukocytes 10 cc. of urine was collected at the time of the culture and examined in a fresh state. The specimen was slowly centrifuged for two minutes and the un-

stained sediment was examined microscopically under the 4-mm. dry objective, using a cover slip; the average number of cells per field was noted. None of the 36 patients with sterile urine in any dilution had any leukocytes in the urinary sediment. Of the 14 with nonsterile urines, the 5 whose urines yielded growth in all dilutions showed no white or red cells in 2, rare white and red cells in 1, a few white and red cells in 1, and 1 or 2 white cells and 5 or 6 red cells in 1. Of the 5 with urines that were sterile except in the 5-cc. dilutions, 2 showed no cells, 2 occasional white cells, and 1 a few white and red cells. Of the 4 whose urines yielded bacteria in the 1-cc. and 5-cc. dilutions but not in the 1-drop plate, 2 showed occasional white and red cells, 1 showed 1 to 3 white and red cells, and 1 showed 1 to 3 white cells and 3 to 5 red cells. It should be noted that white cells were found alone only twice — both times when the urine was sterile except in the 5-cc. dilution. In all other cases either there were no white cells or they were mixed with red cells. In the face of this evidence it must be concluded that what cellular evidence of bacteriuria there was in these subjects without genitourinary disease was either caused by the trauma of catheterization or was so slight as to be insignificant.

Table 4. *Number of Cases for Each Type of Organism.*

Organism	Type of Spinal Injury						Total Cases
	Cervical		Thoracolumbar		Cauda-equinal		
	Living	Dead	Living	Dead	Living	Dead	
P. vulgaris	15	1	8	5	7	0	36
Esch. coli	19	3	6	6	8	0	42
Enterococci	14	2	6	4	6	0	32
Alpha-hemolytic streptococci	16	2	5	4	10	0	37
Staphylococci	15	2	5	3	4	0	29
Other streptococci	5	1	3	0	1	0	10
Ps. pyocyanus	5	1	2	2	3	0	13
Diphtheroids	8	0	2	4	2	0	16
Miscellaneous	19	2	9	7	7	0	44
No growth	11	1	2	1	1	0	16

Table 5. *Results of Urinary Cultures in 50 Persons without Genitourinary Disease.*

Organism	Amount of Urine			
	1 drop	1 cc.	5 cc.	All amounts
All types:	5 (10%)	4 (8%)	5 (10%)	14 (28%)
Esch. coli	1	1	1	
Alpha-hemolytic streptococci	1	5	5	
Staph. albus	4	5	5	
Staph. citreus	2	0	0	
Diphtheroids	0	0	6	
No growth				36 (72%)

Relation Between an Indwelling Catheter and Bacteriuria

It has been proved over and over again that, in the absence of other complications, the presence of a foreign body in the urinary bladder usually prevents or at least delays recovery from any cystitis that may be present. Inasmuch as tidal drainage used in patients with cord injuries prevents puddling and retention of urine, and because it was possible to select patients who had been well up to the onset of their bladder disability, which could be fixed accurately from the point of view of time, we were in an excellent position to estimate the effect of an inlying catheter, uncomplicated by any other factors, on what to all intents and purposes was a normal bladder. It was found that under such circumstances all patients with an inlying catheter had easily culturable bacteriuria by the end of the first seventy-two hours.

Four cases were studied in detail. One patient was first catheterized after ten hours of retention traceable to a cervical-cord injury. He was put on tidal drainage at that time. Cultures taken twelve and twenty-four hours afterward showed no growth. One taken at seventy-two hours showed a ++++ growth of *Esch. coli*. During the sterile period 5 to 15 white cells were present in repeated urinary examinations. The second patient was catheterized one hour after injury. The bladder was atonic, and there was no growth on culture. After four days of tidal drainage a ++++ growth of *Staph. aureus*, *P. vulgaris* and enterococci was cultured. There were a few white cells in both specimens. The third patient was first cultured after having been on tidal drainage for the twelve hours immediately following the accident, again at the end of another twelve hours and lastly at the end of forty-eight and seventy-two hours after the institution of tidal drainage. All cultures were sterile except the last, which showed a ++++ growth of *Staph. albus*. The first three specimens had from ten to forty white cells, and the last was loaded with them. The fourth patient had had an atonic bladder and retention for twelve hours. A urine culture taken at that time was sterile. He was placed on tidal drainage and recultured at the end of another forty-eight hours. There was ++ growth of *Esch. coli* and *Staph. albus*. Neither specimen showed any significant number of white cells.

It is thus apparent that the presence of an indwelling catheter, if it is left in place for seventy-two hours or longer, is enough to produce a culturable bacteriuria.

Bacteriuria and Clinical Infection in the Presence of Tidal Drainage

In the light of the reduction, by the use of tidal drainage,[1] in the mortality and morbidity from the sepsis of the genitourinary tract previously associated with spinal-cord injuries, and because there is no doubt that the chief function of tidal drainage is to eliminate puddling and retention of urine in the bladder, the inevitable bacteriuria referred to above need not and should not lead to significant clinical evidence of infection of the genitourinary tract despite the continued use of an indwelling catheter in patients with spinal-cord injuries.

Seventeen patients were selected for a detailed study of the relation between bacteriuria and clinical evidence of infection while tidal drainage was being used. These were patients seen early in our experience. All were treated with a relatively inefficient form of tidal-drainage apparatus. They were chosen for that reason and because it was thought that they exemplified the least favorable aspects of the problem. Ninety-four observations (cultures and urine examinations) were made, the number ranging from sixteen on 1 patient to one on each of 3 others, with an average of five and a half. The commonest bacteria present were *P. vulgaris*, alpha-hemolytic streptococcus and *Esch. coli*. These were present forty-seven, forty-four and thirty-five times, respectively. However, if 2 patients who included twenty-two positive *P. vulgaris* cultures between them are excluded, the incidences change, becoming twenty-five, thirty-two and twenty-two, respectively. *Staph. aureus* (14), *Ps. pyocyaneus* (11), enterococci (11) and *Staph. albus* (10) came next. Six cultures showed no growth, and other bacteria occurred so infrequently as to be of no significance. This and subsequent experience has led us to believe that no matter what bacteria are originally present, the predominant infection will in a short time be such as to produce and maintain an alkaline urine in spite of all efforts to change it.

These same cases were analyzed in an attempt to find out whether the number of white cells in the urine specimen gave any clue to the amount of culturable bacteriuria. Seventy-five observations were made. An average of 10 white cells per high-power field in a centrifuged specimen was taken as the maximum normal. Only men were included. Among those with sterile specimens 3 showed fewer and 3 more than 10 white cells, the maximum being 40. Of those with ++, +++ and ++++ growths in the cultures, 40 specimens had 10 or fewer white cells and 25 of these had 3 or under. Twenty-nine samples showed 10 or more cells, 10 being described as "loaded." Eight others showed 40 or more cells per field. It appears from this that, provided that the patient is being treated with tidal drainage, culturable bacteriuria to the amount of ++++ is not necessarily accompanied by any rise in the white-cell content of the urine. *Per contra*, cell counts of 40 or over are associated with +++ or ++++ bacteriuria.

A study, under the same conditions, of the temperature reaction and the presence of chills showed that clinical signs of an infection are always accompanied by gross pus or more than 100 cells per field with clumping, and a heavy growth of bacteria, which usually consists of *P. vulgaris* or *Esch. coli*.

In the light of these data it is apparent that bacteriuria always accompanies an inlying catheter after seventy-two hours of use, but that its presence does not necessarily mean infection of any part of the genitourinary tract. Moreover, although bacteriuria is recognizable only by culture, infection of the genitourinary tract, if it is being treated by tidal drainage, is most easily and quickly diagnosed by a study of the temperature chart, the history of the onset of the disease and the number of white cells in a centrifuged specimen of urine.

Sterilization of Urine

Attempts have been made over a period of six years to sterilize the urine of patients with spinal-cord injuries who are necessarily being treated by tidal drainage. These attempts were divided into two parts. The first was concerned with sterilization by the oral or parenteral administration of appropriate drugs and by hand irrigation of the bladder. The tidal-drainage apparatus was not used for the latter purpose because it was not then equipped to irrigate the bladder to any significant degree. The other and more recent attempts endeavored to provide sterilization by altering the chemistry of the bladder urine or by introducing antiseptic irrigating fluids into the bladder at regular intervals by means of a new type of tidal-drainage apparatus that was capable of irrigating the bladder efficiently.[1]

Mandelic acid was tried first. This was a consistent failure because acidification of the urine proved to be impossible in the face of the predominant infective agents and the necessary presence of the inlying catheter. Sulfanilamide and sulfathiazole were then tried in the light of the enthusiastic reports from Johns Hopkins Hospital.[2] Pure cultures of the predominant bacteria were made, their susceptibility to the sulfonamides was demonstrated in vitro, and the necessary lethal concentration of the drug was determined. In most cases this concentration proved to be so high that it virtually meant the elimination of fluids from the diet. Such urinary concentration together with an already existing bacteriuria and an inlying catheter led in every case (it was tried about fifteen times on various patients) to severe ureteropyelitis, regression of the neurologic status and marked impairment of the general condition to the

point where a dangerous illness developed. In certain cases the bacteria could not be killed even in vitro by the drugs. Salvarsan was tried intravenously in another group of patients suffering from what were believed from the descriptions in the literature to be susceptible infections but was a failure in every case. Urotropin by mouth was not tried. Hand irrigation of the bladder at four-to-twelve hour intervals was also practiced using suspensions of sulfanilamide, sulfathiazole and sulfadiazine, and 1:500 and 1:300 dilutions of an aqueous iodine solution (Lugol's). The sulfonamides were complete failures. If the iodine solution was instilled into the bladder and left there for five minutes, it could be demonstrated that the iodine was all absorbed, and indeed in one case symptoms of iodism appeared. The urine, however, was not sterilized. Daily irrigations were no more successful. By this time certain of the earlier patients who had had pyelitis and bacteriuria during their stay in the hospital but whose bladders had returned to normal before their discharge had had urine cultures made on them at various intervals after permanent removal of the inlying catheter. In every case except 2, and in spite of the failure of previous medication, these patients' urines became sterile without any further treatment other than the removal of the catheter, and all remained so. Such end results have been reported elsewhere by one of us,[1] and are introduced here only to emphasize the failure of these attempts to sterilize the urine when the inlying catheter remains in the bladder.

At about the time of these experiments MacNeill and Bowler[3] published their modification of the tidal-drainage apparatus. This provided efficient bladder irrigation. It was also drawn to our attention that potassium permanganate — which was the irrigating solution then in use — was alkaline and therefore not suitable for control of the bacteria that flourished in an alkaline urine. The tidal-drainage apparatus was therefore redesigned and a 0.5 per cent solution of acetic acid was substituted for the permanganate. The culturable bacteria were reduced in numbers, and with a stronger solution of acetic acid the urine could be rendered mildly acid, but it could not be sterilized. Certain urines that tended to throw down phosphate crystals could be made clearer, but the bacteria were still present and remained until the inlying catheter was withdrawn, after which, if the bladder was either normal or of reflex type, they disappeared without anything further being done. Before this conclusion was reached, aqueous iodine, all strengths of acetic acid solution up to 5 per cent and suspensions of sulfathiazole and sulfadiazine had been used without any effect except to produce salivation and mild iodism in 2 patients. No urines were sterilized by any of these solutions. Clinical evidence of pyelitis and cystitis dropped off sharply, however, because of the greater efficiency of the tidal-drainage apparatus. The most significant findings of all this investigation, so far as the bacteriology was concerned, were two. One was that male urethras that are deprived by the presence of an inlying catheter of the irrigation and mechanical cleansing they ordinarily receive whenever the bladder is normally emptied are a constant source, particularly at every fresh catheterization, of reinfection of the bladder urine. The other is that the tidal-drainage apparatus itself reinfects the bladder urine if it is not completely dismantled, cleaned and sterilized once a week.

For the last two years no attempt has been made in this clinic to alter the bacteriuria that is always present in association with the use of tidal drainage in patients with a spinal-cord injury. All but one of such patients who have left the hospital during this period have had sterile urines provided that the indwelling catheter is no longer in place. Their genitourinary tracts have been otherwise normal and the function has been appropriate to the cord lesion in every case. With the use of the present-day tidal-drainage apparatus as further modified by Stewart[4] as well as by Cone and Bridgers,[5] the insistence on weekly cystometrograms, the use of small catheters and the avoidance of all instrumentation of the bladder, the occurrence of pyelitis, ureteritis and cystitis has ceased to be a significant problem except in the presence of a renal or bladder stone. When any such infections have occurred, they have been brought under control in every case without the use of drugs by mouth and by the proper adjustment of the tidal-drainage apparatus and the administration of large quantities (5000 cc. every twenty-four hours) of fluids by mouth, through a stomach tube or intravenously. A renal stone developed in 1 case, and a bladder stone in 2. All these stones were removed surgically. We are therefore convinced that administration of the sulfonamides or any of the other so-called "urinary antiseptics" by mouth or as an irrigating fluid in the bladder cannot control the bacteriuria that always accompanies an inlying catheter as used in the treatment with tidal drainage of patients with spinal-cord injuries. Moreover, we have satisfied ourselves that this bacteriuria is harmless and disappears with permanent withdrawal of the catheter, and that if pyelitis, ureteritis or cystitis does develop in the course of treating such a patient, such an infection promptly clears up following either the removal of any stone that may be present or the adjustment of the apparatus and the ingestion of adequate fluids.

Summary and Conclusions

A satisfactory method of making a urine culture is described.

Asymptomatic bacteriuria may be present in a normal, active person without his knowledge and without the production of symptoms.

The presence of an indwelling urethral catheter is always accompanied by bacteriuria by the end of seventy-two hours.

Patients with spinal-cord injuries who are treated with tidal drainage have an alkaline urine that cannot be acidified.

Infection of the urinary tract as distinct from bacteriuria in such patients is best recognized by the classic signs. These are the onset and progress of the disease, the study of the urine and a sudden rise in the temperature, usually accompanied by a chill.

In our experience sterilization of the urine in the presence of an indwelling catheter used as part of the tidal-drainage apparatus in treating patients with cord injuries has been impossible except by withdrawal of the catheter, and is unnecessary provided that the latest-type apparatus is used and is properly adjusted to the bladder it is serving.

Infection of the urinary tract as evidenced by the symptoms and signs of pyelitis, ureteritis and cystitis in a patient with a spinal-cord injury who is being treated by tidal drainage is best controlled by proper adjustment of the apparatus, bed rest and the administration of large amounts of fluid, preferably by mouth.

Patients who have had a spinal-cord injury and recover to be discharged from the hospital can expect to have a normal genitourinary tract with normal function and without bacteriuria unless they have had a transection of the cord, a renal or bladder stone, a draining periurethral abscess or a lesion that has produced permanent physiologic or anatomic denervation of the bladder.

If such a patient has had a transected spinal cord, he can expect a reflex bladder without bacteriuria and without the need for an indwelling catheter under ordinary circumstances.

If such a patient has had a physiologic or anatomic denervation of the bladder as the result of injury, he can expect a shrunken, useless bladder with bacteriuria and probably recurrent bouts of pyelitis.

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TUBERCULOSIS OF THE LOWER LOBE

Emil Z. Ossen, M.D.*

QUINCY, MASSACHUSETTS

THE lower lobe of the lung as the origin of reinfection tuberculosis has been the subject of discussion from time to time in the past. It has never been treated as an entity in textbooks and in all probability does not deserve to be. However, because of its comparative infrequency in routine admissions to sanatoriums and consequently its much rarer appearance in general practice, there has been a tendency on the part of physicians to ignore its existence. Within the last few years three noteworthy clinical studies have been reported, calling attention once again to this syndrome, its possible pathogenesis and the other factors that are peculiar to manifest tuberculous disease in this area.[1-3]

True basal lesions—that is, those found just above the diaphragm—are extremely rare, but tuberculous lesions located in the upper portion of the lower lobe are not infrequently observed. In fact, as far back as 1888 the latter location was commented on by Fowler,[4] who wrote that the apex of the lower lobe was second in vulnerability to the extreme apex itself. Since then others have shown that this site is not an unusual location for early cavities.

A study of the literature shows that the reported incidence of adult-type or reinfection-type tuberculosis of the lower lobe varies considerably. It ranges from 0.003 per cent of sanatorium admissions, as recorded by Reisner,[1] to 5.6 per cent for men and 10.0 per cent for women, as reported by Viswanathan.[5] In this country it varies between 0.5 and 4.0 per cent of sanatorium admissions, with the latter figure representative of the incidence in female patients.[6-11] It is generally accepted that the frequency is greater among women than among men, on the right side as compared with the left and in the younger age groups as compared with the older ones,[3] and that race and nationality seem to play no part.

The material available for this report was accumulated over a six-year period (1931 to 1937) in which

*Assistant physician, Beth Israel Hospital, Boston; member of Courtesy Staff, Quincy City Hospital; associate member of staff, Milton Hospital.

some 700 admissions occurred at the Norfolk County Sanatorium. The 14 cases represent 2 per cent of all admissions during this period.

In most of the available reports the authors state that their series consist of cases in which the manifest clinical tuberculosis is believed to have begun in the lower lobe. Many writers add that some of these cases have small nodular or fibrotic lesions in one of the apices, but because the presenting and predominant disease is in the lower lobe, they consider the other lesions inactive or obsolete and hence of no consequence. The material gathered for this report deals with the same type of case, but the presence of contralateral or ipsilateral involvement outside the lower lobe has been recognized in one or the other apex. Although this is a small series and thus not properly suited for statistical use, an analysis of these two groups presents data that are deemed worthy of consideration.

Three cases were not included in this series. One was that of a granite worker over sixty years old who had unquestionable evidence of silicosis and in whom a tuberculous cavity was first noted in the left lower lobe. In a series of over 75 cases of silicotuberculosis there were 3 in which the tuberculous cavity of infiltrate seemed to begin in the right middle lobe. In such cases, where two diseases resemble each other closely, it is difficult to determine in which locality the tuberculous process first becomes clinically manifest, although the majority

TABLE 1. *Summary of Data.*

Case No.	Sex	Age yr.	Contact With Tuberculosis	Side Affected	Reaction of Sputum	Type of Onset	Complication	Treatment	Result (1943)
Pure Type									
1	M	19	Mother and 2 siblings	Left	Positive	Acute	None	Pneumothorax	Disease arrested (10 yr.)
2	F	16	Father	Right	Positive	Acute	None	Pneumothorax and phrenicectomy	Disease arrested (3 yr.)
3	F	17	Brother	Left	Positive	Acute	None	Pneumothorax	Disease arrested (3 yr.)
4	F	19	Mother	Right	Positive (gastric lavage)	Chronic	None	Pneumothorax and phrenicectomy	Disease arrested (4 yr.)
5	F	17	Sister	Right	Positive	Acute	Spread to opposite side	Pneumothorax and phrenicectomy	Patient failing; positive sputum.
6	F	19	Sister	Left	Positive	Acute	None	Bed rest	Disease arrested
7	M	23	None elicited	Right	Positive	Acute	None	Pneumothorax	Disease arrested
8	F	22	Brother	Right	Positive	Acute	Tuberculosis, enteritis	Pneumothorax	Death
Impure Type									
9	F	29		Right	Positive	Chronic	None	Pneumothorax and thoracoplasty	Disease arrested
10	F	33		Right	Positive	Chronic	None	Phrenicectomy and pneumothorax	Patient refused thoracoplasty; positive sputum.
11	F	37		Right	Positive	Chronic	None	Pneumothorax and pneumolysis	Disease arrested
12	F	26		Right	Positive	Chronic	None	Pneumothorax and phrenicectomy	Disease present; negative sputum.
13	F	23		Right	Positive	Chronic	None	Pneumothorax	Disease arrested; recurrence on opposite side (6 yr. later).
14	F	37		Right	Positive	Chronic	None	Pneumothorax and pneumolysis	Negative sputum after pneumothorax

and has been made the basis for dividing the cases into two groups (Table 1). A new classification is not offered, but for the purposes of study the cases have been arbitrarily divided into these two groups and the terms described below have been applied. Furthermore, it is fully realized that x-ray studies are too crude for absolute differentiation of the two groups, but they are justified by the results of the analysis. By making this distinction, a unique approach not hitherto reported is attempted and the results of analysis seem to warrant reporting.

In the first group, designated as "pure," are placed 8 cases in which the x-ray appearance of the lesion was limited entirely to the lower lobe with no visible evidence of obsolete, nodular or fibrotic lesions elsewhere in the lungs. In the second group, designated as "impure," are placed 6 cases in which in addition to the predominant lower-lobe lesions nodular or fibrotic disease, such as described above, was found of silicotic patients develop phthisis in the upper lobes in the same proportion as do those with tuberculosis uncomplicated by silicosis.

The second case was that of a seventy-five-year-old woman who had bronchiectasis of the lower lobe of twenty years' duration. A sputum positive for tubercle bacilli was demonstrated once in a series of more than fifty examinations. After death from congestive heart failure, autopsy disclosed considerable bronchiectasis of the right lower lobe, and just beyond the wall of one of the smaller bronchi a caseous tubercle 1 cm. in diameter was noted. It is difficult to classify this case. The patient did not have active tuberculosis in the accepted sense; a logical explanation is that before death there was softening of an old tuberculous focus, perhaps owing to a bronchiectatic abscess or low-grade pneumonitis with consequent shedding of a few bacilli in the sputum.

The third case was that of a male diabetic patient forty-four years of age who had a small lesion in the apex on the right side. Since the evidence for a lesion of the middle or lower lobe was not clear, this case has been omitted.

Symptomatology

A study of the onset reveals that the cases in the present series are roughly divided into the acute and chronic types. The former, generally associated with the pure type, simulated the onset of pneumonia, whereas the latter was common to the impure type and was most frequently diagnosed as bronchitis or bronchiectasis. Of themselves, no symptoms were found to be pathognomonic of lower-lobe tuberculosis. Sokoloff,[12] however, points out that in his series a distinction in the symptomatology could be noted by early onset of night sweats, which in addition usually affected a limited part of the body—that is, the neck, shoulders or head. He also reported an afternoon fatigue that disappeared with brief rest.

Analysis of this series (Table 2), shows distinct differences with respect to age, sex, side affected and type of onset. As regards the history of tuberculous contact, in the pure group there was a strong family history of tuberculosis and intimate contact, suggesting that these patients had received large and frequent dosages of tubercle bacilli in the past. The majority of them had been separated from their original contacts for many years. This is a not infrequent history in tuberculosis of the upper lobe. In the impure group there was no history of tuberculosis contact, familial or otherwise. This suggests that a small apical lesion is acquired after many years of sporadic or chance infection and becomes arrested or quiescent. At some time later in life, perhaps during an intercurrent respiratory infection, bacilli are set free from this old focus, drain down the right bronchus and are localized in the area of vulnerability (described below), where they thrive and ultimately cause caseation, slough and cavitation. With the development of the cavity, the symptoms bring the lesion to the attention of the patient, who seeks medical advice. The impure type is probably not true lower-lobe disease but what could be more properly termed metastatic lower-lobe tuberculosis. For this group a hypothesis has been advanced to explain the predisposition for the right side and the lower lobe.

Table 2. *Analysis of Series.*

Factor	Pure Type	Impure Type
Sex	6 females; 2 males	6 females
Age	16-23 yr., average 19 yr.	23-37 yr., average 31 yr.
Side affected	5 right; 3 left	6 right
Tubercle bacilli in sputum	All	All
Type of onset	7 acute; 1 chronic	All chronic

It is difficult to explain the numerical preponderance of female over male cases in this and other reported studies. Available statistics reveal that more girls than boys develop manifest tuberculosis during adolescence. Thus, one expects a greater percentage of teen-age girls than of teen-age boys in a sanatorium, and hence a greater opportunity for encountering lower-lobe disease among females than among males. This does not, however, explain why there are not more cases of lower-lobe tuberculosis among men between twenty-five and thirty-five years of age, in which age group the male incidence of tuberculosis is at its highest. Some other explanation than that of age must be sought to explain the localization of basal tuberculosis.

The right side was involved in all the impure cases and in 5 (62 per cent) of the 8 pure cases. This finding is in accord with that of most writers. Eleven of the 12 women had the lesion on the right; in both the men they were equally distributed.

Pathogenesis

Two mechanisms regarding the pathogenesis of the pure group suggest themselves. According to the first of these, the caseous-pneumonic lesion is the result of a bronchiogenic or hematogenous spread from the lymph-node component of the primary infection and the lesion, which is usually situated in the upper lobes, has by chance involved the lower lobe. According to the second mechanism, there is direct extension from the parenchymal component of the primary complex, which is oftenest found in the lower lobe on the right side. Sweany[13] has shown that such a process actually occurs in adolescents or young adults who acquire their primary infection during adolescence. The course in these cases is, however, generally rapid and fulminating. The present series includes no case of this type, with the possible exception of Case 8, in which death from tuberculous enteritis occurred.

The impure cases appear to offer more consistent findings. The universal localization in the lower lobe on the right side in women is the outstanding finding. This is best explained on the basis of a theory developed by Reisner.[1] This theory presupposes an area of marked limitation of motion in the lung, which Tendeloo and Macklin[14] have termed the superoretroradicular area. Roughly, the area is paravertebral and corresponds to the usual location of the apex of the lower lobe. This theory has been worked out in the following manner. The diaphragm plays an important role in the expansion of the lower lobe and the posterior portion of the upper lobe, whereas the costal movements are largely responsible for the expansion of the middle lobe and the anterior part of the upper lobe. In general, therefore, it can be postulated that the effectiveness of diaphragmatic action progressively decreases posteriorly and superiorly and that minimal action is obtained at the area corresponding to the apex of the lower lobe. Men are known to be predominately diaphragmatic breathers,

whereas women are costal breathers; consequently, in the latter normal respiration demands little diaphragmatic excursion, with the result that the lower lobe, particularly its upper portion, is poorly ventilated. One can therefore account for a region in the lung that is relatively inert, poorly aerated and in all probability vulnerable to infection. Furthermore, the right side of the diaphragm is more elevated than the left, owing to the underlying liver, and is in consequence liable to a somewhat lessened excursion. This is particularly so in women, as shown by fluoroscopic examinations of the chest. Reisner[1] adds that the right main bronchus comes off the trachea at a lower angle than does the left main bronchus, and in consequence any spreading bronchiogenic infection more naturally drains to the right than to the left side, thereby coming to rest in this vulnerable area. Since the majority of writers have noted the marked preponderance of tuberculosis in the right lower lobe in women, this theory seems to explain their predilection for lower-lobe disease as compared to that of men.

Medlar and Sasano,[15] working with various strains of tubercle bacilli inoculated intravenously in vaccinated rabbits, noted that cavitating lesions were localized in the dorsal and posterior parts of the lung, which are in the superior portion of the rabbit in the usual position of rest, whereas the lesions in the anterior and ventral portion had cleared. Further experiments, in which the rabbits could be kept in a given position for over half the day, over a long period of time, resulted in earlier death, but examinations revealed a localization of the tuberculosis in the highest part of the lung. These authors note an analogy between this tendency to superior localization and the apical or subapical involvement in the human lung.

Medlar and Sasano frankly admit they do not know why the lesions localized as they did, since there is admittedly no peculiar anatomic structure of the lung that lends itself to progressive infection. Also, an alteration of the lung occurs with a change of posture, since emphysema develops in the rabbit's lungs if it is kept in an upright position over a given period of time.

From these studies, it was obvious that neither inhalation(the natural route) nor allergy with subsequent reinfection is of prime importance in the determination of the localization of the progressive cavitating tuberculous lesion.

It is common knowledge that a considerable proportion of spreads to the lower two thirds of the human lung resolve completely, and when they do not, this is probably due to an overwhelming infection or to extreme virulence of the germ. A progressive basilar infection is therefore always of grave import, especially in the absence of apical or subapical involvement. Medlar and Sasano conclude that higher portions of the lung field are less resistant to tuberculous infection than are the lower portions, and that to obtain localizing cavitating lesions it is necessary to have a certain balance between the virulence and dosage of the tubercle bacilli and the resistance of the host, together with a localizing of the tubercle bacilli in certain areas of lung parenchyma; that allergy alters the tissues only so far as the response is more vigorous or prompt; and that this alteration is but one factor that may lead to a localizing cavitating lesion. The factor of greatest importance seems to be the establishment of a certain balance between host and parasite.

Diagnosis

Lateral as well as conventional x-ray films are necessary before a topographical diagnosis of lower-lobe disease can be entertained. The diagnosis of tuberculosis should not be made unless a positive sputum (or gastric lavage) is obtained. As will be noted, this was demonstrated in every case in the series. This does not mean that a positive sputum will be obtained in every case of lower-lobe tuberculosis when first seen. On the contrary, it may not be possible to obtain one in the first few days or even weeks after onset, especially in the pure type. This is also true of the proliferative or exudative type, which resembles a low-grade pneumonitis persisting over four to six weeks, and in which a strong contact history of tuberculosis can be elicited. In such cases it may take months of sputum and gastric examinations before tubercle bacilli are found.[16,17] Thus, roentgenologically speaking, lower-lobe lesions differ from apical ones in that in the latter a diagnosis of tuberculosis can often be made without a positive sputum, whereas in the former a positive sputum is essential.

In the differential diagnosis another lesion that may cause confusion is an active apical tuberculous lesion in association with a unilateral or bilateral basilar nonspecific bronchiectasis. Although this is a rare combination, it is important that the distinction be made, since the principles of treatment for each condition differ markedly. Bronchography and if necessary bronchoscopy should be carried out if the double condition is suspected. A lead to the diagnosis is the copious quantity of sputum, out of all proportion to the size and number of tuberculous cavities present, as well as the small degree of parenchymal involvement in the face of a positive sputum.

Of particular interest at present are the atypical pneumonias, most frequently basilar in distribution and requiring three to six weeks for resolution. They are, however, usually migratory and bilateral, which differentiates them from tuberculosis by the changing signs and the sequence of events. Serial chest roentgenograms soon rule out this condition. In fact, it cannot be emphasized enough that a single positive x-ray film of the chest is often not only misleading but dangerous.[18] Besides the atypical

pneumonias, one must bear in mind the delayed type of resolving lobar pneumonia due to a pneumococcus, particularly since the right lower lobe is often involved.[19] The time interval required for resolution and the absence of residue differentiate these two conditions. It also helps to differentiate basal pneumonias complicating minimal or obsolete apical tuberculosis from tuberculous spreads.

Lung abscess should not be confused with lower-lobe tuberculosis since most of these abscesses follow surgical procedures, and the others can be ruled out by repeated sputum examinations. The sudden onset, the typical pus and the physical signs also aid in the differentiation.

As for the pulmonary mycoses, coccidioidal infections are a problem peculiar to Southern California and to the San Joaquin Valley in particular. Other fungus infections of the lung can be diagnosed from sputum cultures and the usual bilateral nature of the disease.

Neoplasm of the bronchus may give difficulty if associated with tubercle bacilli in the sputum. I have seen 2 such cases, both of which occurred in men of fifty and over. Age and sex therefore help in differentiating the two conditions. Bronchoscopy usually makes the proper diagnosis possible.

To reiterate, the commonest error is to confuse the pure type with pneumonia and to treat it as such for many weeks. This can largely be avoided if an inquiry concerning a history of tuberculous contact is made and appropriate sputum studies, together with serial x-ray examinations, are carried out in all young people acutely ill with pneumonitis.

The impure type rarely gives any trouble, because the associated evidence of ipsilateral or contralateral apical nodular or fibrotic involvement is practically pathognomonic of tuberculosis. The chest roentgenogram indicates the diagnosis, and studies of the sputum invariably confirm it.

Prognosis and Treatment

The prognosis of lower-lobe tuberculosis does not differ from that of disease elsewhere in the lung, depending in large part on the type of disease present. Productive or proliferative disease has a slow and benign course, whereas caseous pneumonic disease has a high morbidity and mortality if not actively treated. All the cases in the present series were either those of acute caseous pneumonia or of its sequela, the fibrocavernous type.

It is interesting to note that many of the earlier writers give an extremely poor prognosis to all basal lesions. In fact, Dunham and Norton[20] were so impressed by the typical course of these lesions that they called all progressive caseous pneumonic disease, whether or not found in the lower lobe, the basal type. They had a large percentage of Negroes in their series. Today, it is thought that the prognosis largely depends on the type of lesion and not on its location.

The principles of treatment for lower-lobe tuberculosis do not differ from those for other lesions and in consequence open cavities must be closed as quickly as feasible. This means that in the acute pneumonic variety, before artificial pneumothorax can be initiated, bed rest is advised until caseation, sloughing and evacuation of the cavity contents have been accomplished and the surrounding pneumonitis has subsided. Not only are complications avoided by this regimen, but also on occasion one may be rewarded by a closed cavity and conversion of sputum, thus saving the patient years of prolonged collapse therapy. Except for one case, the entire series required a dynamic approach for ultimate control.

In the past, lower-lobe lesions have been a strong indication for interruption of the phrenic nerve, but it has been my experience, as well as that of many other workers, that there is little benefit to be derived from the procedure per se, especially where it is the sole means of providing rest and collapse. In fact, in the presence of acute disease it may constitute a distinct danger, since it may cause atelectasis of the lower lobe. Again, with diaphragmatic paralysis thoracoplasty may be dangerous until the function of the diaphragm returns, since atelectasis has been seen in the presence of an elevated diaphragm following such surgery. It seems certain that the only place for phrenic-nerve paralysis is as an adjunct to an existing pneumothorax or thoracoplasty.

In this series of cases, artificial pneumothorax was somewhat more successful in the pure group than in the impure, owing in large part to the paucity or even absence of adhesions in the former, which allows for more adequate collapse of the underlying lung without the necessity of supplementary procedures. This fact may be presented as presumptive evidence that the onset of the impure type is insidious and the disease of long standing. It is in these cases that one encounters the largest number of adhesions, not only about the base but around the apex.

Extrapleural pneumothorax has no place in this form of disease. Intrapleural pneumolysis should be used as a supplementary procedure to sever adhesions that are preventing the satisfactory collapse of the lung. Thoracoplasty has its place but should not be attempted until after long trial of bed rest and minor collapse procedures. When performed, it generally requires the resection of eleven ribs and often anterior section before closure of the cavity is obtained. More recently the tendency has been to make a bronchoscopic examination of all cases for bronchial lesions, since collapse therapy is of little value in those with ulceration. Lobectomy and pneumonectomy are procedures choice of in

certain of these cases, with complete extirpation of the disease as a possibility.[21]

Summary

An analysis of tuberculous lesions in the lower lobe of the lung is made.

These lesions have been divided into two groups according to roentgenologic differences based on the presence or absence of associated apical involvement.

These two groups, named the "pure" and "impure" types, show distinct differences in sex, age, history of tuberculosis contact, the mode of onset and the side affected.

Theories of localization in the lower lobe are reviewed, and evidence for confirmation of Reisner's hypothesis is presented.

A method of treatment is outlined.

1230 Hancock Street

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MEDICAL PROGRESS

THE PARATHYROID GLANDS AND PARATHORMONE*

ALFRED POPE, M.D.,† AND JOSEPH C. AUB, M.D.‡

IN RECENT years a number of excellent reviews on mineral metabolism and its control by the endocrine glands have appeared. Calcium and phosphorus metabolism was comprehensively reviewed by Schmidt and Greenberg[1] in 1935, and the more recent literature in this field was analyzed by Greenberg[2] in 1939 and by Cohn, Cohn and Aub[3] in 1942. Recent advances in the knowledge of the chemistry of calcification were reviewed by Logan[4] in 1940, the physiology of bone and of certain bone diseases by McLean[5] in 1943, and various aspects of phosphorus metabolism by Guest and Rapoport[6] in 1941 and by McLean[7] in 1942. The literature on the relation of the endocrine glands to calcium metabolism was covered by Campbell and Turner[8] in 1942, and special aspects of this problem have also recently been reviewed, such as the physiology and treatment of parathyroid diseases (Albright[9]), secondary hyperparathyroidism (Anderson[10]), calcium metabolism during pregnancy (Bodansky and Duff[11]), the use of sterols in the treatment of hypoparathyroidism (McLean[12]) and the influence of the endocrine glands, including the parathyroids, on growth and aging by Silberberg and Silberberg.[13] The extensive article by Campbell and Turner[8] not only is a complete review of the literature concerning experimental studies on the parathyroid glands but also includes the report of many original observations on numerous aspects of this subject.

*From the medical laboratories of the Collis P. Huntington Memorial Hospital, Harvard University, at the Massachusetts General Hospital. This is publication No. 587 of the Cancer Commission of Harvard University.

†Teaching fellow in biochemistry and research fellow in medicine, Harvard Medical School.

‡Professor of research medicine, Harvard Medical School; physician, Massachusetts General Hospital.

Experimental Studies

Mode of Action of Parathyroid Hormone

Considerable experimental evidence has been obtained in support both of the original theory of Collip that the chief action of the parathyroid hormone is directly on the solution of calcium salts from bone and of that of Albright, who has postulated that its action consists in promoting the renal excretion of phosphate.

Supportive evidence for the renal action of parathormone was obtained by Goadby and Stacey,[14] who failed to obtain the normal phosphate diuresis in patients with chronic nephritis following injection of parathyroid extract, and by Goadby,[15] who was able to correlate the degree of such phosphate diuresis inversely with the degree of severity of the

renal disease. Tweedy and his associates showed that no rise of the serum calcium level occurs after parathormone injection in bilaterally nephrectomized dogs[16] or rats,[17] that the response is normal in a unilaterally nephrectomized dog,[18] and that nephrectomy protects dogs from the characteristic pathologic changes that develop after overdosage with parathyroid hormone in normal animals.[16, 18] Harrison and Harrison[19] have developed a method for the quantitative determination of the amount of phosphate resorbed from the renal tubules, and have shown that in dogs following parathormone administration there is a decrease in the rate of maximal resorption, with reduction in the level of serum inorganic phosphorus. Induced acidosis resulted in the same reduction in tubular resorption of phosphate as parathormone.[20] Fay, Behrmann and Buck,[21] on the other hand, found no difference in the renal clearance of phosphate and creatinine between normal, hyperparathyroid and parathyroidectomized dogs. Brull and Carbonesco[22] concluded from the results of a cross-circulation experiment that parathyroidectomy reduces the excretion of renal phosphate owing to a purely renal effect. Neufeld and Collip[23] produced renal insufficiency in dogs, rats and cats in a variety of ways and were unable to demonstrate any change in the serum calcium level following the administration of parathyroid extract. These authors also found that in normal animals continuous administration of disodium phosphate with parathormone resulted in the maintenance of normal values of serum calcium and phosphorus. All these findings favor the theory of increased renal excretion of phosphate under the influence of parathyroid hormone.

On the other hand, Ellsworth and Futcher[24] found a rise in the serum calcium level after treatment of nephrectomized dogs with parathyroid extract, and concluded that the renal elimination of phosphorus was not prerequisite to this rise. After similar treatment of chronic nephritic patients a rise in the calcium levels sometimes occurred after twenty-four hours,[14] and in nephrectomized rats similarly treated, although no rise of this level was observed, osteoclastic resorption of bone was demonstrated.[17] Similarly, Seyle[25] found that in rats nephrectomy does not prevent the characteristic osteoclastic resorption of bone that follows administration of parathormone, whereas parathyroidectomy does prevent the much less striking bone changes that result from nephrectomy alone. Logan[26] obtained the typical rise of urinary and fall of serum phosphorus levels after injection of parathyroid extract into normal dogs, but also observed a rise in the serum calcium level within one hour whether or not the phosphorus level was simultaneously lowered. Moreover, twelve to twenty-four hours later both the calcium and phosphorus levels of the serum were elevated. Ingalls, Donaldson and Albright[27] studied the effects of parathormone on nephrectomized rats and found definite decalcification of bone, due specifically to the hormone. McLean and Bloom[28] demonstrated bone salt in the trabeculae of spongy bone of rats and puppies under the influence of parathyroid extract, both being transported to the marrow vessels and within marrow macrophages. Moore,[29] however, did similar experiments in rats and found that deposition of calcium phosphate in the bone marrow was always associated with focal tissue degeneration and similar deposits in other tissues. The effect of an extremely active parathormone preparation on the rate of hydrolysis of glycerophosphate by kidney phosphatase was studied by Wood and Ross[30] who found that the accelerating action of the hormone was nonspecific and no greater than that of serum or egg albumin. Although these studies in no way discredit the theory of increased excretion of renal phosphate under the influence of the parathyroid hormone, they do suggest that the latter may have a direct demineralizing action on the bones as well.

Cantarow and his associates,[31, 32] from a study of the partition of calcium and phosphorus between serum and physiologic saline solution injected into the peritoneal cavity of dogs, have concluded that the fundamental action of the parathyroid hormone is to promote the diffusion of calcium from the blood into the various tissue fluids, the source being the solution of bone salts.

Miscellaneous studies on the action of parathormone include the demonstration of a rise in phosphatase activity of serum[33] and of the long bones.[34, 35] Roche and Filippi[35] believe this to be due to an increase in the concentration of enzyme activators at these sites. Cantarow, Haury and Whitbeck[36] found that in dogs parathormone caused a drop in the serum magnesium level, with a rise in that of the peritoneal fluid. Previously, Tibbetts and Aub[37] had shown that magnesium excretion is normal in hyperparathyroidism, although cure of the disease is accompanied by a temporary fall and parathormone administration by a temporary rise of this element in the urine. Increase in the magnesium intake resulted in an increase in the calcium excretion, and these authors suggest that magnesium may be substituted for calcium in the bones in this disease. Cantarow, Brundage and Housel[38] report hyperproteinemia due to hemoconcentration in experimental hyperparathyroidism in dogs. Shelling, Kajdi and Guth[39] found that after the injection of parathyroid extract into dogs there was a marked initial diuresis with a resultant loss of water and electrolytes, which, if repeated, was followed by the usual syndrome of parathyroid "poisoning," with urinary suppression and death. They were able to prevent the latter condition by replacement of fluid and electrolytes, and concluded from this that de-

hydration is an important element in this experimental syndrome. Intestinal absorption of calcium is not affected by oversecretion of parathyroid hormone.[39] Cantarow, Stewart and Housel[40] have studied the pathologic effects of large doses of parathormone in dogs and report both calcification and extensive degenerative changes in the viscera. Bedinger, Kendrick and Keeton[41] studied the toxic effects of calcium administered intravenously to dogs, and among other observations recorded that parathyroidectomy with a low initial serum calcium level affords no protection against these. Logan, Christensen and Kirklin[42] were able to detect only a very slight rise in the urinary calcium level following injection of thyroid into thyroparathyroidectomized dogs, and believed that this might indicate that the parathyroid glands are necessary for the rise of this level that usually follows such administration, although they also pointed out that the low initial level of serum calcium in these animals might in itself have prevented this characteristic effect of thyroid. Schiffrin[43] has reported the effects of parathormone on the gastric secretion of dogs; these are mainly a reduction of the volume and acidity and an increase of the enzyme concentration. The reverse effects result from thyroparathyroidectomy and are due specifically to the lack of parathyroid hormone.

Relation between Parathyroid Hormone, Vitamin D and Dihydrotachysterol

The relation between the parathyroid hormone, vitamin D and A. T. 10 (dihydrotachysterol) has been extensively studied by Albright and his associates,[44-46] who as a result of their comparison of the action of these agents in hypoparathyroidism and rickets have developed the theory that both vitamin D and A. T. 10 increase the absorption of calcium and that all three substances promote the excretion of phosphorus in the urine, but that vitamin D acts chiefly on calcium absorption, whereas parathyroid hormone acts exclusively on phosphorus excretion. A. T. 10 acts only feebly in its enhancement of calcium absorption but is extremely active in promoting the excretion of urinary phosphorus. Hence it is not antirachitic but is a good therapeutic agent for hypoparathyroidism.

Experimental evidence in support of this thesis has appeared. Thus, Shohl, Fan and Farber[47] reported that nontoxic doses of A.T. 10 prevented rickets in rats due to a low calcium and high phosphorus level but not that due to a high-calcium and low-phosphorus diet. They made the reasonable assumption that it was effective in the former by causing a greater excretion of phosphorus in the urine, thus rendering the diet less rachitogenic. Shohl and Farber[48] then showed that in approximately toxic amounts A.T. 10 nullifies the rachitogenic effects of a high-calcium and low-phosphorus diet, which is evidence that it does promote calcium absorption in large doses and is therefore weakly antirachitic, although only one four-hundredth as active in this respect as vitamin D. Bastenie and Zylberszac[49] found that small doses of A.T. 10 resulted in inhibition of mitoses in the parathyroid glands of rats. They assumed that this effect was secondary to the high level of serum calcium induced by this drug. A similar inhibition of mitoses in the parathyroid glands of rats treated with large doses of A.T. 10 was observed by Campbell and Turner.[8]

Rose and Sunderman[50] studied 5 patients with postoperative parathyroid deficiency and found that A.T. 10 was extremely effective in controlling symptoms and maintaining a normal concentration of serum calcium. Himsworth and Maizels[51] compared the efficacy of vitamin D and that of A.T. 10 in the control of a case of idiopathic hypoparathyroidism. Both were effective, but the former was somewhat more reliable and capable of giving perfect control of the serum calcium level if given in sufficiently large doses. Blum[52] has reported excellent clinical results with the use of this agent for the control of hypoparathyroidism, and Ryan and McCullagh[53] were similarly successful. All these authors found that A.T. 10 alleviated the symptoms of parathyroid insufficiency, promoted the excretion of calcium and phosphorus in the urine and controlled the serum concentrations of these substances. They consider that feeding large amounts of calcium by mouth increases the efficiency of the drug and thereby reduces the dosage of the latter necessary to control the disease.

McLean[12] has reviewed the clinical and experimental evidence on this subject and has concluded that vitamin D and A.T. 10 are equally effective in the control of parathyroid insufficiency, provided that the former is given in adequate amounts, the calcemic dosage being one hundred to two hundred times greater than the antirachitic. McLean[12] concluded that unsatisfactory results obtained with the use of vitamin D as a calcemic agent were due solely to inadequate dosage. A discussion of the relative merits of vitamin D and A. T. 10 in treating hypoparathyroidism was included in a presentation of such cases by Cutting, Wells and Carnes.[54] They found the two drugs about equally efficacious, but one of their patients was definitely refractory to A.T. 10. Sevringhaus and St. John[55] have recently reported on the continuation and confirmation of an earlier study[56] on patients with severe permanent hypoparathyroidism in whom the deficiency was perfectly controlled with vitamin D and calcium salts.

Factors Affecting the Activity of Parathyroid Glands

The pituitary and other endocrine glands. Some attention has been given to the possible elaboration of a parathyrotropic factor by the pituitary gland. Friedgood and McLean[57] found that guinea pigs

injected with anterior-pituitary extract developed significant elevations of the serum calcium level. Although there was no change in the level of serum inorganic phosphorus, they interpreted these results as indicating the presence of a parathyrotropic factor in the anterior-pituitary preparation. A similar interpretation was placed by Ham and Haist[58] on their observation that anterior-pituitary extract produced a large number of mitoses in the parathyroid tissue of dogs. Blumenthal and Loeb[59] found that acid extracts of the anterior pituitary gland, hypophyseal implants and potassium iodide all increased the mitotic activity of the thyroid gland and parathyroid glands of guinea pigs, whereas underfeeding and thyroid produced the reverse effect. On the other hand, Carnes, Osebold and Stoerk[60] observed no evidence of impairment of parathyroid function in hypophysectomized rats. The serum calcium and phosphorus concentrations remained normal even under the stress of a low-calcium diet, and hypophysectomized and parathyroidectomized rats behaved in every way like those with parathyroidectomy alone. Similarly, Snyder and Tweedy[61] were unable to detect any alteration in the serum calcium level and actually found a slight rise in the phosphorus level following treatment of rats with anterior-pituitary extract. In hypophysectomized monkeys Baker[62] found a slight atrophy of the parathyroid glands as measured by size and cell count but no change in the histologic or cytologic characteristics of the cells. Campbell and Turner[8] made extensive studies of the effect of anterior-pituitary extract on the weights and mitotic activities of the parathyroid glands of several species and concluded that the existence of a parathyrotropic factor is highly doubtful. In toads, Schrire[63] found no difference in the effect of injected parathyroid extract on the level of plasma inorganic phosphate between normal and hypophysectomized animals. Thus, evidence for a relation between the parathyroid glands and the anterior pituitary gland is neither consistent nor conclusive. If such a relation exists, it is probably not an extremely close one, for the former appear to be able to function even when the anterior pituitary is removed.

In rats, Bastenie and Zylberszac[64] found that folliculin inhibited and progesterone and castration stimulated the mitotic activity of the parathyroid glands. The folliculin effect was inhibited by progesterone, and the castration effect by folliculin. Treatment with both hormones greatly stimulated mitoses in the parathyroid glands of castrated but not in those of normal rats. Campbell and Turner,[8] on the other hand, observed no change in the mitoses of the parathyroid glands of chicks treated with estradiol benzoate. Nathanson, Brues and Rawson[65] have shown that testosterone stimulates mitoses in the parathyroid glands of rats. Similar effects on the thyroid glands of these animals were observed, and since testosterone in moderate doses is known to stimulate ovarian activity through the intermediation of the pituitary gland, these authors suggested that the observed effect on the parathyroid and thyroid was also via the hypophysis. Campbell and Turner[8] were unable to confirm these findings. Bloom, McLean and Bloom[66] found that parathyroid extract abolished the proliferative endosteal reaction in medullary bone, which is a characteristic phenomenon preparative to new-bone formation following the combined administration of estrogens and androgens in pigeons.

Pregnancy. Bodansky and Duff[11] have stated that somewhat low serum calcium values are to be expected in pregnancy and are not to be regarded as abnormal if not below 8.5 mg. per 100 cc. Severe hypocalcemia means either parathyroid deficiency or nutritional inadequacy and results in skeletal abnormalities in the fetus. These authors regard a slightly high fetal serum calcium level as normal. In studies on rats, they found some demineralization of bones in the presence of normal serum calcium levels, presumably owing to stimulation of the parathyroid glands by a lowered serum calcium level. In parathyroidectomized animals, on the other hand, in which the skeleton showed no changes in density, lowered serum calcium levels did develop, and tetany occurred near term. It was found that pregnancy converted latent into active hypoparathyroidism in these animals, and that this condition could be cured by a high-calcium and low-phosphorus diet. Bodansky[67] studied the mineral metabolism of pregnant women and observed evidence of increase in the size and functional activity of the parathyroid glands such that he characterized pregnancy as a state accompanied by a minor degree of hyperparathyroidism. He found a rise of serum phosphatase activity in the last trimester, accompanied, however, by a slight degree of hypocalcemia and little change in serum inorganic phosphorus. In a similar vein, Sinclair[68] showed that pregnancy resulted in marked hypertrophy of the parathyroid glands of rats and that multiparity had a cumulative action in this respect. The hypertrophy could be prevented by a high-calcium and low-phosphorus diet but was enhanced by a diet low in calcium and rich in phosphorus. Similar effects of pregnancy on the volume of the parathyroid glands of rats were reported by Opper and Thale.[69]

In studying the relation of parathyroid activity to pregnancy in rats, Bodansky and Duff[70] found that parathyroidectomy resulted in diminished fertility and reduction in the number and birth weight of the fetuses. These effects were minimized by feeding a high-calcium and low-phosphorus diet. In addition, the parathyroidectomized animals underwent a prolongation of gestation, showed tetany at term and suffered a high rate of maternal

and fetal mortality. These effects were abolished by a high-calcium and low-phosphorus diet. In another study,[71] pregnant parathyroidectomized rats were again shown to be unable to mobilize calcium from their bones, so that the latter retained their normal pregestational weight and hypocalcemia developed. With a rachitogenic diet with a high calcium-to-phosphorus ratio, the differences in bone weights between the pregnant parathyroidectomized and normal control rats were abolished.

Cantarow, Stewart and Housel[40] noted that in the case of a pregnant dog treated with toxic amounts of parathyroid extract and from which nine normal living fetuses were obtained, none of the characteristic pathologic changes observed in the mother were found in the fetuses, suggesting that the parathyroid hormone cannot pass the placental barrier. Bodansky and Duff,[72] from studies on fetal growth and storage of calcium and phosphorus with varying conditions of diet and parathyroid function in pregnant rats, concluded that fetal growth and mineral storage depend entirely on suitable concentrations of calcium and phosphorus in the maternal blood, which it was assumed are accurately reflected in the fetal blood as well. Sinclair[73] found that the parathyroid glands of fetal rats were twice as large in proportion to the body weight as those of adults and were affected by the diet of the mother as a result of changes in her serum calcium or phosphorus level. A diet with a normal ratio of calcium to phosphorus caused enlargement of maternal parathyroid glands, and one with more calcium and less phosphorus tended to suppress changes in both maternal and fetal glands. Such a diet, however, was effective therapeutically after maternal parathyroidectomy. A normal diet to which aluminum acetate was added to reduce phosphate absorption was equally effective under these circumstances. The parathyroid glands of fetal rats were depressed by a high serum calcium or inorganic phosphorus level in the mother. Sinclair found the total weight of the tissue of all the parathyroid glands in fetal animals to be only 5 per cent of that of adults, so that it is probable that pregnancy can afford little protection against the consequences of parathyroidectomy in the mother. It appears clear from these as well as previous studies that pregnancy exerts a great strain on the parathyroid calcium system of the mother, and that this is a period of human life when most careful attention should be given to the calcium and phosphorus content of the diet.

Diet and serum calcium level. Baumann and Sprinson[74] have produced experimental hyperparathyroidism in rabbits by feeding a high-phosphorus and low-calcium diet. The parathyroid glands enlarged with hypertrophy of the cells, and an increase in the amount of circulating parathyroid hormone was suggested by results obtained with the technic of Hamilton and Schwartz. Ham, Littner, Drake, Robertson and Tisdall[75] concluded from their experiments that parathyroid hypertrophy occurs only in low-calcium, not in low-phosphorus, rickets and that it is a function only of the serum calcium level. They interpreted their results as indicating that hypocalcemia, not hyperphosphatemia, is the factor that stimulates parathyroid activity. DeRobertis,[76] on the other hand, has reported that parathyroid hypertrophy, with enlargement and hyperplasia of the cells whose cytologic characteristics become suggestive of marked functional activity, occurs both in rats with low-calcium and in those with low-phosphorus rickets, although the effect is more striking in the former. Similar studies on rats by Carnes, Pappenheimer and Stoerk[77] also revealed that an increase in parathyroid volume occurs on a low-calcium and a decrease on a low-phosphorus diet. When the calcium of the diet was maintained at a constant value, the parathyroid volume was approximately proportional to the amount of dietary phosphorus. The giving of viosterol led to a rise of both serum calcium and phosphorus with a low-phosphorus diet and enhanced the diminution in size of the parathyroid glands. This agent, however, caused an inhibition of the parathyroid enlargement obtained with a low-calcium diet.

Patt and his associates[78, 79] studied the effects of oxalate and of perfusion of the parathyroid glands with decalcified and normal blood on the serum calcium of normal and parathyroidectomized dogs. They concluded that a lowering of the serum calcium level directly stimulates the glands to produce more hormone. Selye[25] noted that parathyroid extract exhibited its usual action in rats previously subjected to partial thyroidectomy or partial hepatectomy, and concluded that the activity of this hormone is not affected by either the liver or the thyroid gland.

An interesting corollary to the effect of diet on the functional activity of the parathyroid glands is the effect of the latter on the mineral appetite of experimental animals. The work of Richter and his associates has shown that the appetite of rats for calcium lactate[80] and other calcium salt solutions[81] is markedly increased by parathyroidectomy, this change being reversed by parathyroid implants,[80] the injection of large amounts of parathormone or the addition to the diet of various materials rich in vitamin D or of A.T. 10.[82] An increase in the appetite for strontium and magnesium salts and an aversion to disodium phosphate solution were also observed following parathyroidectomy.[81] Richter and Birmingham[82] have utilized this appetite method for the bioassay of various substances having an effect on the metabolism of calcium. Wilens and Waller,[83] using the method of Richter,[80] showed that partially nephrectomized rats voluntarily consume increased

amounts of water and the same amount of calcium as preoperatively but decreased amounts of phosphorus. Parathyroidectomized rats increase their calcium and decrease their phosphorus intake, and such animals subjected to partial nephrectomy as well consume an even greater amount of calcium and small amounts of phosphorus.

The kidneys and renal function. The fact that overactivity of the parathyroid glands can produce renal damage has always been of interest, for here is a nephritis produced by one's own secretions. Renal insufficiency may also produce an enlargement of the parathyroid glands, and additional work on this subject has recently been reported. The investigations of Donohue, Spingarn and Pappenheimer[84] showed that partially nephrectomized rats exhibited an increase in the calcium of the remaining renal substance. This was apparently associated with an observed coincident parathyroid enlargement, for it could be prevented by parathyroidectomy. Duguid[85] found that in rats with chronic nephritis due to a high-phosphate, high-vitamin D diet, parathyroid hypertrophy occurred, but since it was found also in animals on such a diet that did not develop renal changes, he concluded that it was the result of a disturbance of phosphorus metabolism and that the relation to nephritis was still uncertain. Chown and his co-workers[86, 87] have studied the renal pathologic changes that develop after administration of parathyroid extract to rats, and believe that they result from calcium deposition both inside and outside of the nephrons, causing obstruction with either atrophic changes or tubular dilatation. The gross lesions observed fell into three categories: cystic dilatation of the tubules, irregular dilatation of the pelvis and chronic focal nephritis. The authors suggest that disturbances in mineral metabolism may be the background for some clinical cases of polycystic kidneys and pyelonephritis.

The Parathyroid Glands and Growth, Repair of Fractures and So Forth

In an extensive study of the effects of parathyroid extracts on the skeletons of growing rats, Burrows[88] found that the hormone caused a retardation of growth and hypoplasia of the parathyroid tissue. On the skeleton the early effects consisted of the classic type of demineralization and the production of characteristic osteitis fibrosa. If administration of the extract was continued, a reversal of this phenomenon was observed, and marked osteoblastic activity brought about a state akin to marble bone disease. Later this effect also tended to diminish, and the bones to return to an essentially normal state. The author has discussed the possible significance of these findings.

Roche and Mourgue[89] have reported that in pigeons with experimental fractures treated with vitamin D_3 or parathyroid hormone, although there was no acceleration of callus formation, there was a significant increase in the bone salt content of the calluses of the treated pigeons over that of the calluses of the untreated controls. In the parathyroid-treated birds mild generalized skeletal demineralization occurred. These authors discuss the therapeutic implications of these findings in the treatment of fractures. Silberberg and Silberberg[90] have recently shown that in mice parathyroid hormone causes hypertrophy, calcification and breakdown of growing epiphyseal cartilage plates. The hormone results in osteoblastic but not in cartilaginous proliferation. Since there was acceleration of epiphyseal closure, the authors concluded that the hormone speeds up the characteristic changes observed in the normal aging process of the skeleton. In old mice with united epiphyses, calcification of inactive cartilage and increased bone formation occurred after parathormone treatment. Similar effects were obtained with the use of calcium gluconate, but combination of the latter with parathormone, although producing a marked increase in bone formation, had no effect on the changes typical of skeletal aging. These observations are interesting, but it must be borne in mind that the reactions of the bones in rats and birds are not the same as those observed in dogs and men.

The Nature of Parathyroid Hormone

Ross and Wood[91] have developed a method for preparing a parathyroid extract that apparently consists of relatively pure parathyroid hormone and that has triple the potency of all previous extracts. Ultracentrifugation showed the presence of two gross molecular species, the molecular weight of one being in the neighborhood of 20,000 and that of the other between 500,000 and 1,000,000. After complete sedimentation of the latter, 50 per cent of the hormonal activity was retained in the mother liquor, suggesting that the smaller molecule is the parathyroid hormone. Pepsin digestion of the whole extract destroyed its activity, ultraviolet absorption studies revealed no chromophoric prosthetic group, and the preparation was stable to electrodialysis, showing that the hormone has no loosely bound polar groups of low molecular weight. These studies therefore confirm the previously suspected protein nature of the parathyroid hormone, which is further strengthened by the studies of Wood and Ross[92] on the ketene acetylation of the hormone, the result of which is complete inactivation, not reversed by subsequent hydrolysis. From this the authors conclude that free amino groups are necessary for the physiologic activity of the hormone.

Clinical Aspects

Hypoparathyroidism

Drake, Albright, Bauer and Castleman[93] have discussed the criteria necessary for making the

diagnosis of chronic idiopathic hypoparathyroidism and consider that the following clinical findings are necessary prerequisites: a low serum calcium level, a high serum inorganic phosphorus level, a normal skeleton by roentgenography and absence of all signs of renal insufficiency. These authors review all the available proved cases of the disease and discuss possible etiologic factors. The pathologic findings in 1 of the 2 proved cases in which these are available are cited, and include complete replacement of all the epithelial cells of the parathyroid glands by fat. In the case with postmortem findings reported by Cantarow, Stewart and Morgan,[94] no parathyroid tissue was identified.

McQuarrie, Hansen and Zeigler[95] studied factors affecting tetany production in a case of idiopathic hypoparathyroidism apart from the level of serum calcium. They found that a low-mineral diet increased the convulsive tendency as provoked by various kinds of stimuli, whereas a high-mineral diet had the opposite effect even without changes in the levels of serum calcium and phosphorus. Hyperventilation induced tetany during feeding of a low-mineral but not of a high-mineral diet. Tetany produced by the antidiuretic effect of posterior-pituitary extract was lessened by addition of salt, which presumably cut down the dilution of the extracellular fluid due to water retention. The authors concluded that in hypoparathyroidism the convulsive tendency is due to more than a low serum calcium level. This is in line with the findings of Evans, Szurek and Kern[96] in surviving parathyroidectomized dogs. These investigators found that such animals remained in latent survival with low serum calcium and high serum phosphorus levels without showing signs of tetany, and concluded that some adjustment in neuromuscular irritability must occur so that it becomes normal in spite of an abnormal electrolyte pattern in the tissue fluids.

Robertson[97] has reported studies on calcium and phosphorus metabolism in cases of postoperative tetany. He found the usual fall in the urinary phosphorus level and elevation of the serum phosphorus level with a drop in both serum and urinary calcium levels, but noted that a fall of the urinary phosphorus level might also occur in uncomplicated thyroidectomy. He also observed in a patient with a serum calcium level of 5.5 mg. per 100 cc. that a normal ratio of fecal to urinary calcium excretion was maintained. This appeared to him to render unlikely the theory that a serum calcium level of about 8.5 mg. per 100 cc. is the renal threshold level for its excretion.

Albright, Burnett, Parson and Sulkowitch[98] state that in the case of a patient with hypoparathyroidism whom they studied the ingestion of aluminum hydroxide caused a lowering of the serum phosphorus level and an elevation of the serum calcium level, the effect presumably being due to decreased phosphorus absorption as a result of the formation of insoluble aluminum phosphate compounds in the bowel.

Several examples of the not uncommon trophic disturbances in tissue of ectodermal origin, including skin lesions, loss of nails and hair and cataract formation, in association with hypoparathyroidism have been reported.[99, 100] Albright, Burnett, Smith and Parson[101] have called attention to a syndrome that they term "pseudohypoparathyroidism" in which the classic clinical and laboratory manifestations of parathyroid insufficiency are present, but in which the essential disturbance is apparently not a lack of parathyroid hormone but rather a failure of end-organs to respond normally to it, since the changes are not reversed by its administration and phosphate diuresis similarly fails to occur. In 1 of 3 such patients studied, normal parathyroid tissue was observed at biopsy. Recently Sutphen, Albright and McCune[102] have reported on the remarkable occurrence of hypoparathyroidism in 3 siblings; in 2 of these cases the disease was associated with widespread moniliasis, and presumably also in the third. Two other cases of association of these diseases were cited, together with 2 cases of associated moniliasis and Addison's disease, in 1 of which there was also hypoparathyroidism. The times of onset of symptoms in these cases suggested that the moniliasis preceded the parathyroid insufficiency. The authors have discussed the possible etiologic significance and relations of these unusual observations.

Hyperparathyroidism

An enlightening résumé of the historical development of knowledge concerning this disease may be found in a recent article by Cope,[103] which also includes an excellent discussion of the two types of pathologic changes that may result in clinical hyperparathyroidism, either adenoma or hyperplasia of the glands. Soffer and Cohn[104] have prepared a review of the literature on primary and secondary hyperparathyroidism, together with a presentation of 5 primary and 4 secondary examples of this disease. One of their cases is of special interest in that the patient apparently had a primary adenoma with hyperparathyroidism that resulted in renal damage and chronic renal disease, the latter, in turn, leading to secondary hyperplasia of the other parathyroid glands. A similar case was studied by Downs and Scott,[105] who were able to reconstruct such a clinical course on the basis of autopsy findings. Snapper[106] has presented an analysis of 3 cases of parathyroid adenoma, 1 of which was of interest because of the finding of a low urinary calcium in combination with the usual biochemical changes associated with hyperparathyroidism. This was attributed to a probable superimposed vitamin D deficiency. Lage and Greene[107] have reported 13 cases of hyper-

parathyroidism from the Middle Western states, an area in which this disease is considered a great rarity. Anspach and Clifton[108] studied 2 cases of parathyroid adenoma in children. In 1 case the onset of the disorder was at three months of age, the youngest such patient known. Another unique feature reported was relief of symptoms and good recalcification of the skeleton following x-radiation of the neck. Jacox, King and Bailey[109, 110] studied a patient with clinical hyperparathyroidism and advanced bone lesions in whom no parathyroid tumor or hyperplasia could be demonstrated surgically and in whom some recalcification of the skeleton, improvement in blood chemical findings and symptomatic relief followed x-radiation of the neck. The patient subsequently died of renal failure, apparently secondary to calculus formation and obstruction of the urinary tract. At autopsy no parathyroid tissue was identified, presumably because of the radiation therapy. It is difficult to account for the fact that the patient terminally still exhibited the blood findings characteristic of hyperparathyroidism. Cope[111, 112] has discussed the surgical management of hyperparathyroidism and laid stress on the specialized knowledge, training and technics involved. An analysis of the distribution of parathyroid tissue, together with observations concerning recognition of its normal and abnormal states and details concerning the surgical removal of diseased glands, are included, as well as a description of the two-stage exploratory procedure used in such cases at the Massachusetts General Hospital. In these operations an initial exploration of the neck and posterior mediastinum is made, and if no parathyroid adenoma or hyperplasia is discovered, search for a tumor in the anterior mediastinum is made at a second session. Three cases of parathyroid adenoma, 2 with unusually located tumors, were reported by Cochrane,[113] whose results led him to suggest the possible efficacy of partial as against complete removal of such lesions. Meyer and Ragins[114] have reported the clinical and pathological findings in a remarkable case of proved parathyroid carcinoma with hyperparathyroidism, fibrocystic disease and renal lithiasis, all three of which conditions improved after excision of the original tumor but reappeared with recurrence of the lesion and the development of metastases. This is an extremely rare condition.

Hansman and Carr Fraser[115] found that in patients with hyperthyroidism generally, but not invariably, there was an associated negative calcium-and-phosphorus balance that could not be correlated with the change in metabolic rate and was unaffected by Lugol's solution. The balance was, however, rendered normal by radiation therapy. These findings led them to conclude that hyperfunction of the thyroid gland and that of the parathyroid glands are often associated, and that hyperplastic parathyroid cells are radiosensitive. A review of such cases has been presented in connection with the report of a case by Miller and Evans[116] of simultaneous thyroid hyperplasia and parathyroid adenoma proved pathologically. A topic of interest in connection with hyperparathyroidism is the finding by Klendshoj and Koepf[117] of a high acid as well as a high alkaline phosphatase level in the serum of a patient proved to have this disease. This is the only reported example of another disease in which the acid phosphatase level was elevated to the same extent as occurs in carcinoma of the prostate with skeletal metastases. The fact that the presenting symptoms of hyperparathyroidism may be the result of changes in the oral cavity has been brought out by Strock[118] in a discussion of the dental symptoms that may be associated with this disorder.

The subject of secondary hyperparathyroidism has been well reviewed by Anderson.[10] Herbert, Miller and Richardson[119] have studied a case of chronic renal disease with secondary parathyroid hyperplasia, decalcification of bone and metastatic calcification and have reviewed similar cases. They have attempted to set a standard for the saturation level of serum calcium and phosphorus above which metastatic calcification may be expected to occur. This they anticipate only in cases such as the one presented in which the combination of renal disease and secondary hyperparathyroidism produced an elevated serum phosphorus level together with a normal or high serum calcium level. Ginzler and Jaffe,[120] however, have concluded that the osseous lesions of chronic renal disease are usually the result of acidosis rather than of hyperfunction of the parathyroid glands, which in most cases were only mildly hyperplastic. The problem of secondary hyperparathyroidism produced by obstructive lesions of the urinary tract in children has been discussed by Harrison,[121] who reports clinical observations and the results of treatment of 5 such patients.

Albright, Burnett, Cope and Parson[122] have published an excellent short discussion of their views concerning the active metabolism of bone and the fundamental physiologic disturbances underlying the development of osteitis fibrosa, osteoporosis and osteomalacia. They point out that although the serum calcium, phosphorus and phosphatase values are normal in osteoporosis, since there is hypercalcinuria, renal damage may ensue, and hypercalcemia may develop, especially if the rate of calcium excretion is insufficient to keep up with that of demineralization of the bones. Under these circumstances a mistaken diagnosis of hyperparathyroidism is likely to be made, and these authors have presented a case illustrating this possibility.

* * *

From the foregoing discussion it should be clear that in the last few years considerable progress has been made in the understanding of both the normal and the pathologic physiology of the parathyroid

glands. Experimental studies have indicated that the parathyroid hormone probably acts both to promote the renal excretion of inorganic phosphorus and to bring about directly the solution of bone salts. Clinical and physiologic investigations have greatly clarified the modes of action and relations of parathyroid hormone, vitamin D and A. T. 10. The treatment of hypoparathyroidism has been rendered simple and effective, and the surgical management of hyperparathyroidism placed on a sound basis.

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Correction. In the report on medical progress, "Hematology," by Dr. William Dameshek, which appeared in the April 27 issue of the *Journal*, the word "donor's," which appears in lines 4 and 7 of the second column, on page 517, should be replaced by the word "recipient's."

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30231

PRESENTATION OF CASE

First admission. A thirty-four-year-old woman was admitted to the hospital because of jaundice and fatigue.

About one year before admission, the patient was sent to the Out Patient Department because of two positive Hinton tests. There was no history of primary or secondary syphilis. Repeat Wassermann and Hinton tests were positive. X-ray studies of the chest and cerebrospinal fluid examinations were negative. Physical examination was also entirely negative. Treatment with bismuth and subcarbonate was started, and she received twelve doses of 0.2 gm. each, followed by eight injections of Mapharsen of 0.03–0.04 gm. each. After each injection of Mapharsen she had nausea and vomiting for one or two days and felt weak. She was given another course of bismuth subcarbonate (0.2 gm.) and seven intravenous injections of neoarsphenamine (0.45 gm.). Her general weakness, tiredness, headache, various joint aches and occasional nausea and vomiting continued and became constant, and she was forced to give up her job. She had no appetite and lost about 28 pounds in weight. In the last few weeks of the treatment she began to notice a steadily increasing yellowish pigmentation of the skin. All her symptoms seemed to become aggravated and she was admitted to the hospital.

Examination showed a thin, alert woman. The skin was dry and "jaundiced," the color being described as yellowish brown on the face, dorsum of hands and knees and brown on the palmar creases. There was a "bismuth line" around the teeth. Small patches of ecchymoses and hemorrhagic spots were seen on the back and on the inner surfaces of the lower extremities. There was yellowish pigmentation of the scleras and conjunctivas. Generalized enlargement of the cervical, axillary and epitrochlear lymph nodes was noted, but examination was otherwise essentially normal.

The blood pressure was 100 systolic, 70 diastolic. The temperature was 98°F., the pulse 90, and the respirations 20.

*On leave of absence.

Examination of the blood showed a red-cell count of 4,650,000, with a hemoglobin of 14.2 gm. The white-cell count was 9900, with 66 per cent neutrophils. The urine was acid and had a specific gravity of 1.030. A foam test was positive for bile; there was a + test for acetone and a rare hyaline cast. The stools were light yellow to brown and occasionally guaiac positive. The blood protein was 5.9 gm. per 100 cc. The prothrombin time was 20 seconds (normal, 20 seconds), and the hematocrit 51. The van den Bergh was 6.4 mg. per 100 cc. direct, and 9.3 mg. indirect. The blood chloride was 83.6 milliequiv. per liter. Repeat chloride determinations were 96.7 and 91.4 milliequiv. per liter. The sodium was 128.2 milliequiv. per liter; the blood sugar was 82 mg. per 100 cc. The carbon dioxide combining power was 21.8 millimols per liter. A glucose tolerance test revealed a fasting blood sugar of 36 mg. per 100 cc., 162 mg. at the end of one hour, 85 mg. at the end of two hours, and 64, 59 and 43 mg. at subsequent successive half-hour periods. A cephalin flocculation test was + in twenty-four and forty-eight hours.

The patient continued to vomit and was given daily infusions of glucose and saline solutions and several transfusions. The electrolyte levels were sustained by this method, but she continued to take and retain little by mouth. The vomitus varied in amount, was guaiac negative and contained free hydrochloric acid. A mousy odor was noted in the breath. A blue-gray streaking of the hard palate and the undersurface of the tongue and patches on the buccal mucosa were seen at the end of the first week. A plain film of the abdomen showed no areas of calcification. A 17-ketosteroid determination showed that 2.8 mg. was excreted in twenty-four hours. After the first week she received daily doses of sodium acid phosphate, Hykinone and sodium chloride. The vomiting stopped, and she was able to take and retain a high-calorie, high-vitamin diet. Although still jaundiced, the van den Bergh dropped to 1.2 mg. direct and 1.8 mg. indirect and the cephalin flocculation time became zero; the blood sodium remained at about 128 milliequiv. per liter. The patient was finally discharged two months after admission.

Second admission (three months later). Following discharge the patient did well, had no nausea or vomiting and gained about 3 pounds. She had considerable craving for salt, but whether this was real or merely because she had been advised to use more salt could not be ascertained. The pigmentation disappeared from the scleras but was persistent in the skin. For the first time in her life, however, she was bothered by the cold and her hands and feet blanched on exposure to cold. About two months after discharge she had a mild upper respiratory infection, felt extremely tired and depressed and had no appetite. She recovered from this episode, however, and for the next three weeks

felt fairly well. About a week before readmission, she contracted another cold. In the next few days she became gradually weaker and more tired. Two days before admission she commenced to vomit after eating or drinking. This progressed and became almost constant. One hour before entry she developed a dull, steady, slight pain in the epigastrium, which extended under the sternum.

Physical examination showed an emaciated woman who was vomiting and in marked distress. The skin was dark tan, especially over the exposed parts. Some dark-gray pigmentation and stippling of the hard palate were noted. There were tachycardia and gallop rhythm at the apex. Examination was otherwise the same as on the first admission.

The blood pressure was 80 systolic, 70 diastolic. The temperature was 98.6°F., the pulse 110, and the respirations 20.

Examination of the blood showed a red-cell count of 4,400,000, with 12 gm. of hemoglobin. The white-cell count was 9200, with 55 per cent neutrophils. The urine had a specific gravity of 1.018 and a pH of 5.0 and gave a ++++ test for acetone; there were occasional hyaline casts. One stool was brown and guaiac positive. The blood chloride was 97 milliequiv. per liter, the sodium 125.2 milliequiv. The carbon dioxide combining power was 19.0 millimols per liter. The nonprotein nitrogen was 18 mg. per 100 cc., and the protein 6 gm. The van den Bergh was normal.

The patient was given 10 cc. of adrenocortical extract intramuscularly, followed by 20 cc. in 3000 cc. of 10 per cent dextrose in normal saline. In the next two or three days the blood chloride became 107.4 milliequiv. and the sodium 135.9 milliequiv. per liter. A diuresis test showed the volume of the night specimen to be larger than that of the morning specimen. On the fifth day the blood chloride was 101.7 milliequiv. per liter. The blood urea nitrogen was 5.6 mg. per 100 cc. The urine chloride was 116 milliequiv. per liter, and the urine urea 172 mg. per 100 cc. The daytime volume of urine was 130 cc., and the night volume 200 cc. She had three intramuscular injections of eschatin (adrenocortical extract) on the fourth, fifth and sixth hospital days, following which she improved considerably and the vomiting ceased. The stool was guaiac negative. A 17-ketosteroid assay showed an excretion of 2.8 mg. in twenty-four hours. The cephalin flocculation time was normal. The prothrombin time was 20 seconds (normal, 22 seconds). The hematocrit was 34.7. A spinal tap was normal. She was discharged on the seventeenth hospital day on an added salt intake (5 gm. daily).

Final admission (six days later). Following discharge she remained well for three days. She had no nausea, vomiting, fatigue or lethargy. On the fourth day she complained of tightness across the chest, which persisted. She had no pain, cough or weakness. The following night she could not sleep because of a "feeling of impending disaster." Thirteen hours before entry the temperature was 101°F. She was listless and began to vomit. Throughout the day she became progressively weaker and extremely "tired." The temperature dropped to normal. One hour before admission the extremities turned blue, she was cold and clammy, the pulse could not be obtained, and she became stuporous.

Examination showed a cyanotic moribund patient with a spastic right arm held in flexion. She was frothing at the mouth, and the jaws were tightly clenched. She moved all extremities when stimulated. Respirations were shallow. The heart sounds could not be heard, and the pulse and blood pressure could not be obtained. Immediately after admission 25 cc. of Wilson's adrenocortical extract was given intravenously, along with 10 per cent of dextrose in saline. In fifteen minutes she became active. She was given oxygen and another 10 cc. of the extract intravenously, followed by a similar dose intramuscularly. She received about 1250 cc. of the dextrose solution in the course of two hours. At the end of that period she suddenly choked, frothed slightly at the mouth, gave a few gasps and stopped breathing.

Differential Diagnosis

Dr. George W. Thorn*: A thirty-three-year-old woman was first seen because of two positive Hinton tests, which were subsequently checked. Antisyphilitic treatment — two courses of bismuth, one of Mapharsen and one of neoarsphenamine — was then instituted. At the end of a year she became jaundiced, was admitted to the hospital, stayed two months, went home for three months, came back for a relatively short period, went out again, returned and died. The questions are: Was syphilis the sole cause of her trouble? Were heavy metals the sole cause of her trouble? Did heavy metal intoxication complicate syphilitic infection? Was there some complication totally independent of heavy-metal therapy and syphilis?

The first point to take up is the jaundice. Jaundice as we know, occurs in approximately 1 to 2 per cent of patients with syphilis who are treated with arsenicals. It is about seven times as frequent in patients who are treated with arsenicals for syphilis as it is in patients with syphilis who do not receive arsenical treatment. In other words, there is seven times the chance of having jaundice due to heavy-metal therapy as compared with the possibility of jaundice on the basis of syphilis alone.

The jaundice reactions that occur in syphilitic patients with heavy-metal intoxication are interesting and can be placed in three groups. The first is the jaundice that immediately follows the *first injection* of neoarsphenamine, associated with a Jarisch–Herxheimer reaction. This type of jaun-

*Hersey Professor of the Theory and Practice of Physic, Harvard Medical School; physician-in-chief, Peter Bent Brigham Hospital.

dice is usually not serious; it is transient and is supposedly due to the killing of large numbers of spirochetes. Another type of jaundice is that associated with "ninth-day erythema." In this reaction jaundice with chills and fever develops ten to twelve hours after the second or third injection of neoarsphenamine and it is quite readily diagnosed. It is not due to a hepatitis. In the majority of patients the jaundice disappears. This type has all the appearances and all the laboratory findings characteristic of obstructive jaundice. The phosphatase is over 10 Bodansky units, and the cholesterol over 250 mg.; the cephalin flocculation is low or negative. Hanger and Gutman[1] are responsible for describing this particular type of jaundice due to neoarsphenamine. It is different from the third type of jaundice or ordinary hepatitis, which one sees at any time during the course of neoarsphenamine, and which may occur as long as two, three or even four months following the cessation of heavy-metal therapy.

One other point before we embark on the chemical studies is the significance of the positive Hinton tests. We all know that false positives occasionally occur. One of the most illuminating pieces of information that has come out of the Army recently is that a primary take following smallpox vaccination is probably associated with one of the highest incidences of falsely positive Wassermann or Hinton reactions. From 10 to 20 per cent of persons develop a positive reaction after vaccination. One to two months later, however, the titer falls off and the reaction becomes negative. This is true of other infections that are associated with falsely positive serologic tests.

The important thing to me in a patient who has no physical evidence of syphilis and no history of primary or secondary disease is to be sure that the positive test represents syphilis. I think we can assume that it does in this case, because positive tests were recorded over some period of time. In the absence of a primary or secondary lesion, the Army and Navy follow a person with positive tests for a month or two before assuming that they are due to syphilis.

How much of this patient's illness may we attribute to heavy-metal therapy? What type of jaundice did she have? The ninth-day erythema, or the more frequent hepatitis? It is difficult to say. Certainly she did not give the characteristic picture of ninth-day erythema. Nausea and vomiting associated with jaundice suggest that she had some reaction in the liver to heavy-metal therapy. That is my first thought, and we have no evidence, as we go along, of any other disturbance that would cause jaundice except for the courses of bismuth. It is rather interesting that some patients treated with bismuth alone develop jaundice. In most cases, however, this occurs after ten or twelve injections, and may appear one or two weeks after the discontinuance of therapy. I suspect that this woman had a relatively mild degree of parenchymal involvement of the liver. One wonders whether the reaction was delayed, whether the patient was sensitive to the drug, or whether she had some underlying disease that gave her poor resistance to the injections. It is interesting that no jaundice developed until a second course of neoarsphenamine was given. We know that neoarsphenamine causes jaundice much more frequently than does Mapharsen, and logically, the addition of neoarsphenamine to the treatment may have been responsible for the jaundice.

Considerable interest centers around the serum chloride level of 83.6 milliequiv. per liter. What can produce that? Are low electrolytes caused by adrenal insufficiency? That is our problem. Did she have adrenal insufficiency before she was given treatment or did the toxicity of a heavy metal cause it? Of the patients with syphilis and Addison's disease, relatively few prove to have syphilis of the adrenal glands, although it is referred to in every textbook and article that I know of. Most reports discuss patients with symptoms of Addison's disease who, when given arsenical treatment, become asymptomatic, and it is concluded, without pathological data, that the patient had syphilis of the adrenal glands. In my experience, patients with Addison's disease do not tolerate antisyphilitic treatment, and I am quite convinced that this patient did not have Addison's disease at the time she was given the last injection of neoarsphenamine. I should expect such therapy to have induced collapse if she really had severe adrenal insufficiency.

If Addison's disease is not the cause of the disorder of sodium and chloride, what could have induced these changes? Low sodium and chloride can occur in patients who are vomiting and in patients who have a high concentration of organic acids in the blood, which is consistent with liver disease. The glucose tolerance test was normal, unlike that in patients with Addison's disease, when glucose absorption is disturbed.

The pigmentation is striking, but pigmentation is also typical of bismuth poisoning and helps us little in this difficult diagnosis.

She was given a vitamin K preparation. I do not know why the sodium acid phosphate was given. The jaundice improved, and she was discharged. For three months she had considerable craving for salt, and then was readmitted. She had had two colds or two upper respiratory infections, but she came back with a temperature of 98.6°F. — a patient with Addison's disease in moderate collapse has hypothermia. The pulse rate was 110. The patient was extremely weak and tired, which suggests possible myocardial change. The blood pressure was low. An interesting point is that while she was at home the blood chloride was 97 milliequiv., and the sodium 125 milliequiv. One

never sees this discrepancy in Addison's disease, and that is suggestive, if the chemical values are true, of a type of renal disease in which the chloride is retained in excess of sodium. If you give sodium chloride to a patient of this type you raise the sodium and chloride milliequivalent for milliequivalent. You will notice later that the chloride came up to 107 milliequiv. and the sodium to 135 milliequiv. I should say that a patient with Addison's disease associated with heavy-metal poisoning would not do well at home on salt, without hormone therapy.

There are two other features of great interest. She had free hydrochloric acid in the stomach. One rarely sees that in a patient with Addison's disease. The second point is that on the second admission there was a ++++ test for acetone in the urine, which is rarely if ever seen in Addison's disease or in a severe liver disturbance. At that time, the van den Bergh was normal, the jaundice had disappeared, and she was given adrenocortical extract and intravenous glucose solution. Since 3 liters of glucose and saline solution was given with the extract, one cannot say that the latter was the effective agent. A Kepler–Power[2] water test was done. In adrenal insufficiency there is a tendency for the urea to be higher in the blood than in the urine. Patients with Addison's disease do not have good diuresis following water injection. The ketosteroids are interesting — they were low, but a good many patients have low ketosteroid excretion. If the ketosteroids are normal, one can immediately rule out Addison's disease. If low, in any patient who is hospitalized and sick, one cannot prove Addison's disease. The prothrombin time was normal. The cephalin flocculation test was normal. These constitute evidence against a severe grade of hepatitis.

The patient went home for two or three days, became listless, with a feeling of impending death, came to the hospital in extremis, had a temperature of 101°F. and died. Just before the final episode she became alert enough to respond when glucose and adrenocortical extract were given intravenously. That merely suggests, to my mind, the hydrating effects of glucose, especially a temporary improvement of the cerebral state so that she could realize where she was. Although there are a considerable number of points in favor of adrenal insufficiency, I hesitate to make that diagnosis in this patient because of several points: the presence of hydrochloric acid in the stomach, the ++++ test for acetone in the urine and the disproportion between the chloride and sodium levels. The pigmentation is compatible, the excretion of ketosteroids is compatible, and the glucose-tolerance test and the clinical course fit in with many cases. I do not believe that she had Addison's disease before heavy metals were administered; if so, she would have had a much severer reaction.

Regarding hepatitis, I think that the patient had evidence of liver damage, but that it was not sufficient to cause death. She must have had a considerable amount of functioning liver tissue to have a ++++ test for acetone in the urine.

Regarding the possibility of a renal lesion, arsphenamine and bismuth might have caused it. There was evidence of tubular degeneration, but the final urine had a specific gravity of 1.018, with only a few casts. So far as the urine findings alone are concerned, one cannot say that she had nephrosis, but the response to sodium and chloride — the prompt rise in chloride and the slower drop in sodium — and the fact that the sodium chloride levels could be maintained on the intravenous fluid alone strongly suggest difficulty in sodium and chloride excretion on the part of the kidneys.

The blood pressure was low, and the pulse rate was rapid. I suppose that there were small areas of focal myocarditis and swelling of the myocardial muscle fibers. As a terminal event she may have had heart failure or even a pulmonary infarct. She had definite evidence of a terminal change in the brain, as demonstrated by the paralysis. I am a little disturbed with respect to the bone marrow. She may have had some depression of the bone marrow, because the final counts were lower than the earlier ones, but the bone-marrow depression was not marked.

Am I permitted to see the heart films? I should like to know whether the heart was small or normal.

Dr. Laurence L. Robbins: It is certainly small, although many normal people have hearts of this size. This was taken in the Out Patient Department one year before the first admission.

Dr. Thorn: There was no subsequent change in the heart size?

Dr. Robbins: No. The second film was taken three months before the first admission and showed no change. We have no later films.

Dr. Thorn: A small heart is consistent with adrenal insufficiency and certainly against extensive myocardial change, and against anything in the way of renal lesion. It almost makes me change my mind in this case.

If the heart became definitely larger, one would consider a myocardial or renal defect. If the heart remained small, one would certainly make a diagnosis of adrenal insufficiency. The heart size is one of the most important things to follow in a patient with adrenal insufficiency. One can tell more about the state of the circulation from the size of the heart than from any other factor. I must add to my diagnosis the question of Addison's disease.

Dr. Oliver Cope: In contrast to clinical observations, there is no change in the output of hydrochloric acid in the stomach in experimental adrenal insufficiency. In the surgical research laboratories of this hospital the dog has been observed to secrete hydrochloric acid (pH 0.88) throughout the development of acute adrenal insufficiency, even terminally.

It is, to my mind, entirely a matter of stimulation, which is difficult to obtain in the dog. The patient with Addison's disease also has anorexia and vomiting. When the dog is fed artificially by stomach tube it puts out hydrochloric acid even with a blood chloride level below 80 milliequiv. To my mind, therefore, the presence of hydrochloric acid in the stomach of a patient does not exclude adrenocortical insufficiency.

DR. JACOB LERMAN: When this patient was first admitted, the diagnosis was arsphenamine jaundice or hepatitis. The resident who saw her on various occasions, Dr. Gordon S. Myers, raised the question of Addison's disease because of the peculiar pigmentation in the mouth, plus the low salt in the blood. He thought that the appearance was different from that of bismuth poisoning. That argument went on pro and con between the residents, the interns and the visiting staff for some time, and finally the consensus was swayed against Addison's disease, primarily because of the presence of ketosteroids in the urine. The opinion was that any amount of ketosteroids militated against a diagnosis of Addison's disease.

I saw her when she came in the second time. The jaundice had cleared completely, and to me, the picture looked quite characteristic of Addison's disease, with a typical distribution of pigmentation. She was in collapse but responded readily to salt and adrenocortical extracts. We speculated whether bismuth poisoning can play a role in the production of Addison's disease. In the experience of a large syphilitic clinic where large doses of bismuth are given over many years it is extremely rare to find a case of Addison's disease. I therefore threw out bismuth as a factor.

We were particularly convinced of the diagnosis of Addison's disease when she returned in coma and died quickly. Because she had responded at first so quickly to small amounts of adrenocortical extract and of salt intravenously, we thought that she had a mild case of Addison's disease. The various members who saw her believed that the proper treatment was to carry her along on salt and to give extract as indicated. Apparently she was in a much severer stage of the disease than we had anticipated.

CLINICAL DIAGNOSIS

Addison's disease.

DR. THORN'S DIAGNOSES

Healed arsphenamine hepatitis.
Myocardial failure.
Pulmonary infarct.
Tubular changes in kidney (bismuth)?
Addison's disease?

ANATOMICAL DIAGNOSES

Addison's disease.
Tuberculosis of adrenals, bilateral.
Tuberculosis of mesenteric lymph nodes.
Pericarditis, acute fibrinous, with effusion.
Pulmonary edema.
Hydrothorax, bilateral.
Ascites.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Autopsy showed that both adrenal glands were three to four times their normal size, and completely replaced by caseous tuberculosis. The regional nodes were caseous, and there was old tuberculosis in the lungs, both apices being completely scarred. The immediate cause of death was an acute pericarditis with effusion. It is perhaps fortunate for Dr. Thorn that chest films were not taken at the time of the last admission, because the effusion would have caused an enlarged heart shadow. The heart itself was extremely small.

DR. THORN: I have seen six cases of Addison's disease with pericarditis. In one or two of them it was hemorrhagic.

DR. COPE: In these cases was the etiologic agent a streptococcus?

DR. THORN: No cultures were done, and no organisms were seen on smear.

DR. CASTLEMAN: The liver was normal in size, perhaps a bit small, and showed no evidence of hepatitis. The kidneys were essentially normal. We found no anatomic lesions of syphilis.

DR. THORN: The acetone is the most interesting aspect of this case. It is unusual for the urine of a patient with adrenal insufficiency to give a ++++ test. Differential diagnosis could have been made on the response to desoxycorticosterone acetate rather than to sodium chloride, since the latter is nonspecific and helpful in many types of dehydration, whereas the hormone effect is specific.

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CASE 30232

PRESENTATION OF CASE

A sixty-three-year-old night watchman entered the hospital because of cramps in the lower abdomen of five days' duration.

During the year preceding entry, the patient had noticed occasional cramps in the lower abdomen, increasing constipation without melena, slight decrease in the size of the stools and slight weight loss. Five days prior to admission he developed persistent cramps in the lower abdomen and anorexia. He had no bowel movements for the three days preceding entry, except for a small one on the morning of admission. During this time, however, he had

passed gas by rectum but had been aware of increasing retention of gas and distention.

Physical examination showed a well-developed, sallow man in no discomfort. The heart and lungs were normal. The abdomen was distended and tympanitic. Intermittent, high-pitched, peristaltic rushes were heard. A large tympanitic, nontender mass was present in the cecal area. Rectal examination showed a soft palpable mass 7 cm. above the anus.

The blood pressure was 148 systolic, 72 diastolic. The temperature was 98.6°F., the pulse 100, and the respirations 24.

Examination of the blood showed a red-cell count of 4,480,000 and a white-cell count of 10,450. The urine was normal. A blood Hinton test was negative. The stools gave a ++ guaiac test. A plain film of the abdomen showed a large amount of gas in the colon, extending to the lower sigmoid. The cecum was somewhat dilated. Proctoscopy, including the rectum and sigmoid to a point 20 cm. above the anal sphincter, was negative.

On the second hospital day a cecostomy was done. Postoperatively the patient did well. On the third hospital day a barium enema showed a mass in the pelvis, displacing the rectum and sigmoid to the left. The examination was unsatisfactory because of the large amount of gas in the colon. A Miller–Abbott tube was passed. A repeat barium enema showed an annular area of narrowing, extending over a distance of approximately 6 cm., and situated about 3 cm. proximal to the rectosigmoid junction. The margins were shelf-like, and there was ulceration. During fluoroscopic examination only a small amount of barium passed beyond the tumor. After the patient had evacuated some of the barium, the films showed that considerable barium had passed into the descending colon, and there was barium

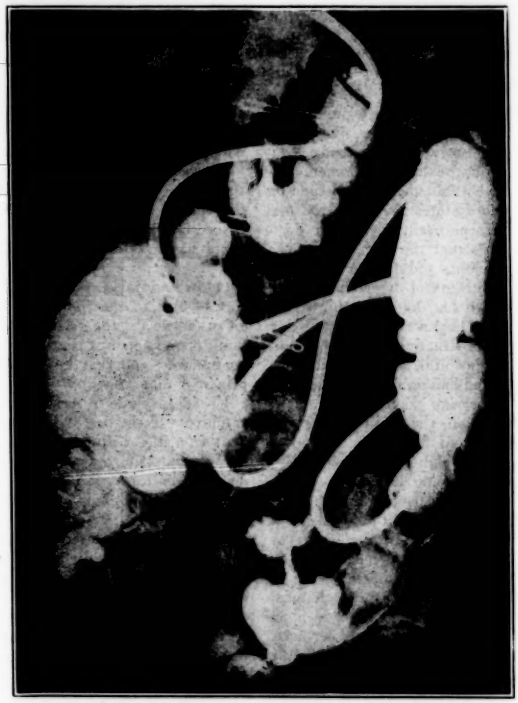

FIGURE 1. *Post-Evacuation Film following a Barium Enema.*
The small arrow points to the lesion in the sigmoid; the large arrow, to barium in the ileum.

in the small intestine (Fig. 1). A mass was present in the right side of the pelvis that displaced the rectum rather markedly to the left.

On the fourteenth hospital day a transverse colostomy was performed. This was opened two days later. There was excellent drainage. Irrigation to the loops was satisfactory. During the course of the next two weeks the patient's general condition improved considerably and he felt and looked much better. On the thirtieth hospital day an operation was performed.

Differential Diagnosis

Dr. E. Parker Hayden: From the beginning this seems to be a typical story of progressive, large-bowel obstruction — a story of increasing constipation and cramps in the lower abdomen over a period of a year, with slight decrease in the size of the stools. The record states that no blood had been noted. One thinks naturally of the two commonest diseases that obstruct the large bowel in a person of this age: carcinoma and diverticulitis. The lack of blood makes one think of diverticulitis. On the other hand, this man had had a slight weight loss, suggesting cancer. There was also the five-day episode of pronounced obstruction, which brought about his entry to the hospital, and the period of three days in which he had had no movement except one small one, but was passing gas by rectum.

On physical examination the patient was described as being sallow, and he had a distended, tympanitic abdomen, with high-pitched peristalsis, suggesting an obstructing lesion based not on inflammation but on a mechanical obstruction somewhere in the colon. In diverticulitis there is, of course, a localized inflammatory process, but the resulting obstructive symptoms are mechanical in nature. There is blocking of the lumen, owing to swelling of the bowel segment, and a real mechanical obstruction develops. The finding that is most difficult to explain is the tympanitic nontender mass in the cecal area. I suppose we can fairly well rule out a distended bladder because of tympany and the location of the mass on the right side.

The first diagnosis that occurs to me in this case is an old appendiceal abscess with sufficient putrefaction in the abscess to produce gas. Now and then a large abscess is tympanitic to percussion, and it may not be tender if it has been present for a long while. On the other hand, since the man had no fever and no increased white-cell count, an abscess seems unlikely.

The man may have had some queer intraperitoneal herniation. I can recall a patient who would fit this description rather well. She had a herniation of the small bowel through an aperture around the cecum, producing a similar picture — a large, freely movable, tympanitic, soft mass in the right lower quadrant. I have never seen one since, but the memory of this one came quickly to mind. This man could have had an intraperitoneal herniation. On the other hand, such a lesion would probably have involved the small bowel, and in that case one would expect symptoms of small-bowel, rather than large-bowel, obstruction. Furthermore, a Miller-Abbott tube was passed.

Another possible explanation is a volvulus of the right colon, which can produce a large tympanitic mass in that area. Yet we have evidence of a definite lesion in the upper sigmoid. If this lesion was 3 cm. proximal to the rectosigmoid junction, it should have been visualized when the proctoscope was passed 20 cm., but one must make allowances for a discrepancy in the estimated distance.

The description of the barium-enema examination, which showed a constricting lesion with shelf-like margins and ulceration, makes it difficult to conclude that this was anything except carcinoma of the descending colon. If there was a carcinoma of the descending colon, this, rather than the appendix, could have perforated and could have produced a big abscess.

One should also consider the possibility of some sort of cyst in the right lower quadrant or pelvis. In other words, the cecal mass may be one of the familiar red herrings that crop up so often in these conferences, and that have nothing to do with the principal diagnosis.

I shall conclude by saying that this woman had a carcinoma of the descending colon. This seems evident from the x-ray description and from what we know about the operative procedures. When one does a cecostomy, it is usually for large-bowel obstruction, although I have seen the operation performed when that did not exist. A transverse colostomy, coming later, suggests that the operator found something in the left colon which he thought he could resect, with an anastomosis. So, influenced by these facts, I think I must make a diagnosis of carcinoma of the descending colon, with acute obstruction of five days' duration. I have no idea what the soft mass was. The diagnosis that fits this picture best is some type of intraperitoneal herniation.

Dr. Benjamin Castleman: Would you like to see the x-ray films?

Dr. Hayden: Yes.

Dr. Milford Schulz: The most pertinent ones were made following cecostomy.

Dr. Hayden: I intended to emphasize the fact that, since the Miller-Abbott tube was used, obstruction in the small bowel seems likely.

Dr. Schulz: Curiously enough the lesion shows best in the routine films rather than in the spot films. There is something peculiar down here. There are several collections of barium that do not seem to be in the colon.

Dr. Hayden: That suggests perforation, with a large abscess cavity and gas.

Clinical Diagnosis

Carcinoma of sigmoid, with ileocolic fistula.

Dr. Hayden's Diagnosis

Carcinoma of descending colon, with obstruction and perforation.
Intraperitoneal small-bowel hernia?

Anatomical Diagnosis

Adenocarcinoma (Grade III) of sigmoid, with ileosigmoidal fistula.

Pathological Discussion

Dr. Castleman: At operation the surgeon felt a large mass in the region of the descending colon that was adherent to loops of small bowel. He was able to separate a few of the loops of small bowel from the mass, but suspecting an ileocolic fistula because of the presence of barium in the small intestine as demonstrated by the x-ray films, he resected the colon and the adjacent small intestine.

We found an annular, 5-cm., ulcerating carcinoma of the sigmoid, which had extended through the serosa and communicated with the ileum by means of a fistulous tract 1.5 cm. long and about 2 mm. in diameter. No cancer was present in the small intestine.

The New England Journal of Medicine

Formerly

The Boston Medical and Surgical Journal

Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Thursday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

ONE HUNDRED AND SIXTY-THIRD ANNIVERSARY

The one hundred and sixty-third anniversary of the Massachusetts Medical Society, held at the Hotel Statler, Boston, on May 22, 23 and 24, proved to be the most successful meeting ever held. Although the total registration — 1440 — was somewhat less than the 1556 members who attended in 1942, it is obvious that the former figure represents a higher percentage of members practicing within the Commonwealth than does the number of two years ago, owing to the absence of approximately 1500 members because of military service.

At the annual meeting of the Council, several matters of general interest were discussed, and appropriate action was taken. The Committee on Membership submitted an exhaustive report covering the admission of graduates of foreign medical schools to the Society; on the basis of this study, the committee stated that no change in the by-laws was indicated, and this recommendation was approved by the Council. The Subcommittee to Meet with the Medical Advisory Committee of the Industrial Accident Board reported that arrangements had been made with insurance companies whereby physicians will be reimbursed for emergency medical care and that it is permissible for a patient to be moved to another hospital where he can be cared for by a physician of his own choice, provided there is assurance that the care will be adequate. The War Participation Committee stated that a program designed to take care of any catastrophic emergency — war or civilian — had been worked out as a co-operative venture by the Society, the American Red Cross and the Massachusetts Committee on Public Safety. After considerable discussion, it was voted to hold over the recommendations of the Postwar Loan Fund Committee until the February meeting of the Council, the consensus being that the reaction of the Society as a whole should be obtained before taking action. Dr. Reginald Fitz, Massachusetts chairman of the Procurement and Assignment Service, reported that approximately 2900 physicians coming under the jurisdiction of his committee were serving with the armed forces, that there had been little evidence of shortage of physicians, that the 9-9-9 plan for interns and residents was functioning satisfactorily and that, by and large, the medical manpower situation had become clarified and well adjusted. On the basis of recommendations by the Committee on a Medical Information Bureau, the Council voted to establish such a bureau at the headquarters of the Society, to appoint a committee to supervise the activities of the bureau and to appropriate the sum of $2500 for the annual maintenance of the bureau. And, finally, the appointment of the Postwar Planning Committee was authorized. The officers elected for the current year are as follows: president, Elmer S. Bagnall; vice-president, Sumner H. Remick;

president-elect, Reginald Fitz; secretary, Michael A. Tighe; treasurer, Eliot Hubbard, Jr.; assistant treasurer, Norman A. Welch; and orator, Frank H. Lahey.

At the annual meeting of the Society, Dr. William H. Robey presented an appreciation of the late treasurer, Charles S. Butler, and the president, Roger I. Lee, reported on the state of the Society. At the close of the meeting, the orator, Joseph C. Aub, delivered the annual oration, entitled "A Toxic Factor in Experimental Traumatic Shock," which will appear in a subsequent issue of the *Journal*.

The annual dinner was well attended, nearly 500 tickets having been sold. The Honorable Leverett Saltonstall, Governor of Massachusetts, took the profession somewhat to task for its failure to make the laymen aware of all that physicians have done and are doing for the public good; he warned that methods to provide good medical care at a reasonable cost must be provided. Bill Cunningham, with his customary forceful style, pleaded for better morale on the home front.

Many excellent papers were presented at the general scientific sessions, and the Shattuck Lecture was given by Dr. Alfred Blalock, surgeon-in-chief, Johns Hopkins Hospital, and professor of surgery, Johns Hopkins University School of Medicine, the title being "A Consideration of Certain Recent Advances in Surgery."

The luncheon meetings of the sections were extremely popular; in fact at that of the Section of Medicine the demand to hear the speaker, Dr. Walter C. Alvarez, of the Mayo Clinic, was so great that the meeting had to be moved from Parlor B into the Georgian Room.

The scientific and technical exhibits were so numerous that the Mezzanine, as well as the Ballroom and Ballroom Assembly, was filled to capacity. The receipts from the rental of booths made an all-time record, a fact that will undoubtedly receive favorable comment from the Treasurer and the Committee on Finance.

Once again, the Society is greatly indebted to Dr. Gordon M. Morrison and his committee, as well as to Robert St. B. Boyd, the executive secretary.

NEWTON HEALTH DEPARTMENT AGAIN WINS AWARD

NEWTON has again received honors for attaining excellence in protecting public health in wartime by being one of the fifty-three cities and counties to receive recognition in the 1943 National Health Honor Roll. The program was sponsored by the United States Chamber of Commerce and the American Public Health Association.

The winners were selected by leading national authorities, who spent weeks grading the reports of participating communities throughout the country. Emphasis was placed on specific measures to control communicable diseases, such as venereal disease, tuberculosis and children's diseases. Sanitation, including protection of milk and food supplies, proper safeguards for maternity care, child health and welfare, effective health education, adequate measures to promote industrial health and other health services were also given primary consideration. Many of the participating communities were war-production centers that have found it necessary to make an inventory of health conditions regarding both wartime health problems and postwar planning.

In commending the winning communities as well as those that participated in the program, the United States Chamber of Commerce said:

> This achievement deserves the highest praise and support and reflects great credit on the health officers, officials, voluntary health organizations, chambers of commerce and other business and civic groups in these localities for giving adequate attention to the wartime health of war workers and citizens.
>
> It is our hope that the records of the 1943 National Health Honor Roll cities and communities will be an incentive and guide to others to build up their health protection services. We hold this an essential home-front contribution to speed the winning of the war and to meet the great problems of postwar readjustment.

The evaluation schedule used in this national program is one of the best possible tools for postwar planning. Its use gives every community exact knowledge of where it stands in health and hospital facilities in connection with adjusting itself to postwar conditions. Communities that make this inventory now are steps ahead of other communities in postwar planning. Armed with definite plans for improvements and expansion, these communities will obviously be in the best position to obtain trained technicians and additional facilities for improving their health programs after the war.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

COOK — Edward M. Cook, M.D., of York Harbor, Maine, died May 20. He was in his forty-sixth year.

Dr. Cook received his degree from Harvard Medical School in 1924. He was a member of the American Medical Association.

His widow, his mother and a son survive.

FLAGG — Harry H. Flagg, M.D., of Charlestown, died May 25. He was in his sixty-fourth year.

Dr. Flagg received his degree from Tufts College Medical School in 1908. He was a member of the American Medical Association and the Charlestown Medical Society.

His widow and two daughters survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

REGULATIONS REGARDING GONORRHEA REVISED

The regulations of the Massachusetts Department of Public Health regarding venereal diseases have recently been revised. Among other changes the regulations have been made applicable to chancroid, granuloma inguinale and lymphogranuloma venereum.

One other change has been the adding of a new paragraph, which reads as follows:

Minimum Requirement for a Negative Diagnosis in Women Who Are Suspected of Having a Gonococcal Infection. Whenever a female is alleged to have been exposed to gonorrhea, or to have been the source of infection of gonorrhea, the department shall require that there be one or more negative cultures of material taken from the urethra and cervical canal, in accordance with the instructions accompanying the outfit, before the department will accept a report that the person is free from infection; said cultures to be done in a laboratory approved by the department.

(NOTE. If, in the physician's judgment, there exists a history of exposure and/or physical signs and symptoms of the disease in the female, regardless of negative laboratory findings, the case should be reported as gonorrhea.)

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1944

RÉSUMÉ

DISEASES	APRIL 1944	APRIL 1943	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	1	3	1
Chancroid	1	*	*
Chicken pox	2792	1136	1286
Diphtheria	19	8	11
Dog bite	920	949	959
Dysentery, bacillary	0	2	7
German measles	397	8658	157
Gonorrhea	319	379	368
Lymphogranuloma venereum	*	*	*
Measles	3490	7282	4012
Meningitis, meningococcal	54	118	7
Meningitis, Pfeiffer-bacillus	4	1	14
Meningitis, pneumococcal	7	5	†
Meningitis, staphylococcal	1	—	†
Meningitis, streptococcal	2	2	†
Meningitis, other forms	2	5	†
Meningitis, undetermined	8	15	†
Mumps	1483	770	785
Pneumonia, lobar	332	360	521
Salmonella infections	5	42	6
Scarlet fever	1737	2579	1172
Syphilis	334	455	479
Tuberculosis, pulmonary	196	253	253
Tuberculosis, other forms	19	17	25
Typhoid fever	4	3	3
Undulant fever	3	3	3
Whooping cough	312	604	798

*Made reportable in December, 1943.

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENT

Diphtheria showed a distinct downward tendency in April although running far ahead of the same month last year. The cases were almost entirely confined to the eastern end of the Commonwealth. Meningococcal meningitis, pleasingly enough, showed a figure less than half that of last April. But it was still nearly eight times the seven-year median.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Amherst, 1; total, 1.

Diphtheria was reported from: Boston, 7; Brockton, 1; Chelmsford, 1; Fitchburg, 2; Lawrence, 4; Lexington, 1; New Bedford, 1; Salem, 1; Somerville, 1; total, 19.

Encephalitis, infectious, was reported from: Longmeadow, 1; total, 1.

Malaria was reported from: Boston, 15; Camp Edwards, 10; Cushing General Hospital, 3; Fort Banks, 20; Fort Devens, 15; Fort Rodman, 3; Haverhill, 1; Swansea, 1; total, 68.

Meningitis, meningococcal, was reported from: Acton, 1; Adams, 1; Andover, 1; Arlington, 1; Ashland, 1; Boston, 12; Bridgewater, 1; Brockton, 1; Cambridge, 1; Camp Edwards, 2; Carver, 1; Charlton, 1; Chelmsford, 1; Easthampton, 1; Fall River, 2; Fort Devens, 1; Framingham, 1; Greenfield, 1; Lowell, 2; Marlboro, 1; Medford, 1; Newton, 1; North Attleboro, 1; Northampton, 1; Norton, 1; Plymouth, 1; Reading, 1; Salem, 1; Somerville, 1; Springfield, 1; Swansea, 1; Wakefield, 1; Waltham, 1; Watertown, 1; Webster, 1; Weymouth, 1; Winthrop, 1; Woburn, 2; Worcester, 1; total 54.

Meningitis, Pfeiffer-bacillus, was reported from: Boston, 1; Brockton, 1; Framingham, 1; Peabody, 1; total, 4.

Meningitis, pneumococcal, was reported from: Holyoke, 1; Lynn, 1; Melrose, 1; Quincy, 1; Springfield, 1; Sutton, 1; Westport, 1; total, 7.

Meningitis, staphylococcal, was reported from: Boston, 1; total, 1.

Meningitis, streptococcal, was reported from: Boston, 2; total, 2.

Meningitis, other forms, was reported from: Rockland, 1; (leptomeningitis) Springfield, 1; (leptomeningitis) Somerville, 1; total, 3.

Meningitis, undetermined, was reported from: Boston, 1; Lowell, 1; Ludlow, 1; Norwell, 1; Paxton, 1; Springfield, 2; Worcester, 1; total, 8.

Salmonella infections were reported from: Boston, 1; Cambridge, 1; Newton, 3; total, 5.

Septic sore throat was reported from: Billerica, 2; Boston, 9; Camp Edwards, 1; Fall River, 1; Haverhill, 1; Hull, 1; Greenfield, 1; Mansfield, 1; Upton, 1; Williamstown, 2; total, 20.

Tetanus was reported from: Hanover, 1; total, 1.

Trichinosis was reported from: Concord, 3; Hadley, 1; total, 4.

Typhoid fever was reported from: Chicopee, 1; Melrose, 1; Quincy, 1; Springfield, 1; total, 4.

Undulant fever was reported from: Cushing General Hospital, 1; Hopedale, 1; Millbury, 1; total, 3.

MISCELLANY

INTRAPLEURAL PNEUMONOLYSIS

The emphasis on early diagnosis of pulmonary tuberculosis would seem to be wasted if effective treatment is unnecessarily postponed. Discriminating selection of cases for collapse therapy, skillful choosing of the appropriate method and prompt employment of the elected procedure are indicated in the interest of all concerned. Pertinent facts are brought out in a recent article (Dailey, J. E. Intrapleural pneumonolysis. *Dis. of Chest* **9**: 492-495, 1943), which is abstracted below:

* * *

It seems generally agreed that at least half the cases of pulmonary tuberculosis require some form of collapse treatment, either reversible or irreversible. Thoracoplasty is the best surgical example of the latter, while the oldest technic devised — pneumothorax — is a good representative of temporary, reversible collapse of the lung.

The chest specialist is the one to select either method after he has evaluated the patient's condition and the stage of his tuberculosis. The mistaken belief that "time heals everything" must give way to acknowledgment that this disease invariably demands immediate consideration and active methods of treatment whenever indicated. In this race against time, the presence of a cavity calls for measures to obliterate it before delay invites a hemorrhage or spread results in a hopeless condition.

Pneumothorax remains the first choice, but is successful in only about half the cases in which it is initially tried. Lack of success may be attributed to adherence of the two pleural surfaces so that collapse of the cavity is impossible or incomplete. Delay in the institution of pneumothorax may allow the parenchymal inflammation to progress and involve the pleura until adhesions form and so defeat later attempts at what should have been a simple collapse procedure.

Formerly, a risky method attempted to stretch or break such adhesions by forcing air into the pleural cavity under positive pressures. Serious complications developed if the adhesion, breaking off near the lung, tore the latter so that a tuberculous or mixed-infection empyema resulted. Serious hemorrhage might follow rupture of a sizeable vessel incorporated in the adhesion. Precious time was often wasted while the hoped-for stretching of the adhesion was awaited. Meanwhile the still unaffected cavity might supply bacilli to cause other cavities elsewhere.

Intrapleural pneumonolysis was designed to transform, where feasible, a poor pneumothorax result into a satisfactory effective collapse. Under local procaine infiltration anesthesia, a special cannula is introduced between the ribs into the pleural space, transmitting a visual instrument not unlike a cystoscope. Through this the operator views the interior and by means of a cautery inserted through a second cannula in another interspace severs the adhesions under direct vision.

Adhesions vary in size and shape and may be multiple. They range from "fiddle string" to short, thick and cylindrical, or may resemble accordion-pleated sheets that radiate in all directions and run all the way from paper-thinness up to bands one or several centimeters in diameter. In using the cautery it is necessary to remember that thicker adhesions may contain lung tissue or large blood vessels and that they may be attached firmly to the aorta, subclavian artery or vital mediastinal structures. Great skill is required to avoid disasters similar to those already listed above as chargeable to stretching and rupture of adhesions.

A skilled operator severs an adhesion as near its parietal extremity as possible, thus protecting the lung while exercising due caution as regards the intercostal structures as well, especially if actual dissection in the latter area proves necessary. In competent hands, backed by adequate experience and judgment when and when not to cut, the operation is a minimal one as regards the patient's discomfort. In less experienced hands, however, it can present dangers exceeding those of almost any other major intrathoracic surgical procedure.

When a pneumothorax is started and adhesions can be seen to interfere with collapse, provided the space is large enough for the surgeon to manipulate his instruments, there is no reason for delay. Besides the well-known hazards of an open cavity, the longer one waits the thicker grows the pleura covering the bands and the greater the difficulty of cutting them.

Very large adhesions may have to be severed partially at one sitting and finished in stages after waiting periods of three or four weeks have intervened. Adhesions too widespread to submit to this method call for abandonment of the unsuccessful pneumothorax and the selection at once of a collapse procedure other than pneumonolysis.

Summary. Remember the time factor and begin active pneumothorax treatment immediately in any patient who has a cavity. Don't wait to see what happens to the case with prolonged bed rest. Too often the realization will be accompanied by disappointment and chagrin.

In about half the cases a pneumothorax will be complicated by adhesions.

Don't attempt to stretch adhesions by means of a positive pressure pneumothorax.

Make an attempt to sever them by intrapleural pneumonolysis — again remembering the importance of time — as soon as possible.

In the hands of an expert, the unfavorable consequences of the operation are insignificant and the complications rare, but when performed by one with little experience, the dangers are very real.

If it is impossible to improve the collapse by pneumonolysis, abandon the pneumothorax and perform a thoracoplasty. — Reprinted from *Tuberculosis Abstracts* (May, 1944).

NOTE

Several appointments to the faculty of Tufts College Medical School have been recently announced. Dr. Norman A. Welch, physician-in-chief at the Carney Hospital, was named professor of clinical medicine. Mr. Manfred Bowditch, director of the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries, was appointed professor of industrial hygiene. Dr. Walter T. Garfield was designated as emeritus professor of dermatology, with Dr. John G. Downing, physician-in-chief of diseases of the skin, Boston City Hospital, succeeding him. Dr. Raymond D. Adams, neuropathologist at the Boston City Hospital, was named lecturer in neurology.

CORRESPONDENCE

RESTORATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held May 17, the Board voted to restore the license to practice medicine in this Commonwealth of Dr. David S. Goodman, 168 Chestnut Street, Chelsea.

H. Quimby Gallupe, M.D., *Secretary*
Board of Registration in Medicine
State House
Boston

NEED FOR NAVAL MEDICAL OFFICERS

To the Editor: A total of 100 qualified physicians and dentists are needed by the Bureau of Medicine and Surgery for assignment to the United States Veterans Administration. The program is open to males not over sixty years of age. Except for those specially nominated by the United States Veterans Administration, rank will be comparable with age and experience. The physical requirements are the same as those established for general appointments, but special waivers may be granted. No indoctrination period is required. Those selected will be assigned to the United States Veterans Administration, and physicians and dentists now thus employed will be assigned, if commissioned, to the Veterans Administration.

It is to be emphasized that the procurement of physicians and dentists for regular service in the Navy is still urgent. Recommendation for this special program will be given only in those cases in which a doctor or dentist is over age, or where a waiver of physical defects not ordinarily granted is required.

As in the case of all medical and dental officer applications, a statement of availability by the Procurement and Assignment Service is required.

H. S. Gidden
Commander MC-V(G), U.S.N.R.
Senior Medical Officer
Office of Naval Officer Assignment
150 Causeway Street
Boston 14

MEDICAL FEES IN RURAL VERMONT

To the Editor: A study of farm economics in Vermont has recently been published (Adams, T. M. *Prices Paid by Vermont Farmers for Goods and Services and Received by Them for Farm Products, 1790–1940; Wages of Vermont Farm Labor, 1780–1940.* 176 pp. Bulletin 507, University of Vermont and State Agricultural College. Burlington, Vermont: 1944). The sources are account books of individuals and business firms in various rural communities of the state. Vermont has the largest rural percentage of population of any state in New England. In 1940, 66 per cent of the people of Vermont were in communities of less than 2500 population, whereas in Massachusetts only 11 per cent lived in rural areas, and in Rhode Island only 8 per cent.

Four fifths of the towns in the state were covered in the search for account books of individuals and business firms.

Four tons of such books and diaries were consulted. The compiler is a member of the faculty of the University of Vermont, and this study was accepted by Cornell University as a thesis for the degree of Doctor of Philosophy.

One of the one hundred and twenty-three lists of prices is that of medical fees from 1800 to 1940, for which a table with eight hundred and forty-six entries appears on pages 58–60. I have abbreviated this table to forty-five entries by taking only the decennial years and only the fees for three types of medical service, namely, an office call, a house visit by day within one mile and an obstetric delivery. The list is as follows:

Date	Office Call	House Visit	Obstetric Delivery
1800	——	$0.25	$2.00
1810	$0.30	0.45	2.00
1820	0.30	0.45	3.00
1830	0.28	0.41	2.83
1840	0.30	0.46	3.12
1850	0.42	0.50	3.00
1860	0.42	0.50	3.00
1870	0.67	0.83	5.00
1880	0.62	0.75	5.00
1890	0.56	0.81	5.00
1900	0.54	0.88	6.14
1910	0.72	1.20	9.75
1920	1.29	1.89	20.00
1930	1.34	2.03	22.44
1940	1.34	2.03	23.15

The table does not give an entry for an office call in 1800. Account books of physicians in eastern New York, which I possess, show that when the fee for a house visit was 25 cents in the early nineteenth century, the average fee for an office call was 18¾ cents. Assuming that the same relation held in neighboring Vermont, the total for the three services was $2.44 in 1800. This total did not double until 1865, and it trebled in 1900. In 1905 the total became four times the original and in 1912 five times the original. In 1925 it first passed ten times the original, and in 1940 it was nearly eleven times what it was in 1800. It is evident that fees in rural medical practice in Vermont increased much more rapidly in the twentieth century than in the nineteenth century. No mileage was charged for a visit within one mile, but rural physicians were accustomed to charge mileage for professional visits at a distance of more than one mile. The rate in Vermont in 1800 was in accord with that in other northern states, being 10 cents per mile. In 1865 the rate became approximately 20 cents, in 1900 approximately 25 cents, in 1916 approximately 30 cents, and in 1925 approximately 35 cents. The fees did not include medicine during the greater part of the nineteenth century; pharmacies were rare except in cities, and the physician furnished the medicines for his patients, for which he made an additional and separate charge. The prices entered in the table are the average from the account books of physicians in each year. The number available varied but was enough to give a fair cross section.

Frederick C. Waite, Ph.D.
Dover, New Hampshire

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Hundred Years of Medicine. By C. D. Haagensen, M.D.; and Wyndham E. B. Lloyd. 8°, cloth, 444 pp., with 42 illustrations. New York: Sheridan House, 1943. $3.75.

This is a story of the medical discoveries of the past century, written in simple terms for the layman. The various diseases and conditions are considered individually, and the work of outstanding figures, such as Virchow, Semmelweiss, Koch, Pasteur, Lister, Ehrlich, Röntgen, Halsted, Cushing, Banting, Minot and Domagk, are emphasized. A bibliography for students is to be found at the end of the work, and the text is well illustrated.

Blood Supply of the Visual Pathway. By Calvin M. Kershner, M.D., M.S. (ophth.). 8°, cloth, 160 pp., with 33 illustrations. Boston: Meador Publishing Company, 1943. $3.00.

This small monograph attempts to gather together in one place in a systematic manner the essential facts displayed in a wide literature, so as to make the anatomical knowledge of value to the ophthalmologist. The work is divided into two parts. In the first, the general arterial supply and the general venous drainage are considered. In part two there are detailed descriptions of the blood supply and drainage of each section of the visual pathway.

Clinical Diagnosis by Laboratory Examinations. By John A. Kolmer, M.S., M.D., Dr.P.H., Sc.D., LL.D., L.H.D., professor of medicine, School of Medicine and School of Dentistry, Temple University, and director, Research Institute of Cutaneous Medicine. 8°, cloth, 1239 pp., with 75 illustrations. New York: D. Appleton-Century Company, 1943. $8.00.

This new work aims to represent fully the clinical interpretations of laboratory examinations and their practical applications in the diagnosis of disease, with a special section on technical methods sufficient for meeting the needs of teaching clinical pathology to medical and dental students. It is divided into three parts: laboratory examinations, divided into twenty-one chapters; the practical applications of laboratory examinations in clinical diagnosis, consisting of twelve chapters; and the technics of laboratory examinations, divided into nine chapters.

Veterinary Bacteriology. By Ival A. Merchant, D.V.M., Ph.D., C.P.H., associate professor of veterinary bacteriology and hygiene, Iowa State College. Second edition. 8°, cloth, 640 pp., with 135 illustrations. Ames, Iowa: The Iowa State College Press, 1942. $6.50.

The second edition of this book has not been extensively revised, because of the exigencies of wartime. The chapter on the genus Streptococcus has been changed more extensively than any other. The fact that the first edition was published in September, 1940, and the second edition in November, 1942, speaks well for the popularity of the work.

The Biochemistry of Malignant Tumors. By Kurt Stern, M.D.; and Robert Willheim, M.D., professor, University of Philippines, Manila. 8°, cloth, 951 pp. Brooklyn, N. Y.: Reference Press, 1943. $12.00.

This special work attempts to cover the relation of cancer to chemistry in the broadest meaning of both words, based on a collection of literature as complete as possible. It is the first publication in English of a treatise on the subject. The arrangement of the material is in line with the general principles of biochemistry. The main emphasis has been placed on the work of the last twenty-five years, and the literature has been systematically covered until the end of 1941. In 1936 the authors published in Vienna a German work of the same character and this book is an amplification of that monograph. Most of the views expressed were formed during a period of more than ten years of joint experimental work in cancer research. Considering the work of others in the field of cancer research, the authors have endeavored to enumerate the facts and also to introduce a critical analysis.

White Blood Cell Differential Tables. By Theodore R. Waugh, M.D., C.M., pathologist-in-chief, Royal Victoria Hospital, associate professor of pathology, McGill University, and consulting pathologist, Montreal Homeopathic Hospital, Montreal, Quebec. 12°, cloth, 126 pp. New York: D. Appleton-Century Company, Incorporated, 1943. $1.60.

Ninety per cent of the space of this small pamphlet is given up to tables for computing rapidly from the differential percentages the number of each type of white blood cell per cubic millimeter of blood. The tables cover the numbers up to 10,000. Preceding the tables there are 15 pages of preliminary descriptive matter.

(*Notices on page xi*)